RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

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Volume 44

January—June 1945

Owned and Published as its Official Journal by
THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

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Vol. 44 JANUARY 1945 No. 1

Tropical Diseases of Interest to the Radiologist[1]

LT. COMDR. L. H. GARLAND, M.C., U.S.N.R.

TROPICAL diseases have been defined as diseases which occur or tend to be more prevalent in tropical and subtropical zones. As a result of modern methods of transportation, however, and the present world conflict, they are seen with increasing frequency in temperate areas. Some of the major factors influencing their usual locale include special climatic conditions essential for the existence of the intermediate hosts or vectors often required for their transmission to man, poor local sanitation, and primitive living conditions. The return of large numbers of infected military and civil personnel from endemic areas may result in a significant incidence of the diseases in this country. In this connection it is well to remember that only three decades ago malaria was a common disease in the United States; typhus is still a common disease in Europe; and cholera and yellow fever are only two generations away as a commonplace in subtropical latitudes.

In the present résumé we will attempt to consider the more significant diseases in the approximate order of their present clinical importance in this country, and will also make brief reference to certain diseases not strictly tropical in nature, but of sufficiently greater incidence in some tropical and semitropical areas to warrant consideration here.

MALARIA

Malaria is probably the most important world-wide disease today (1) and is undoubtedly the major medical problem of the present world war. As has often been noted, "it accelerates the decline of nations and vanquishes more soldiers than the enemy" (2). The radiologist is concerned with the disease in this country chiefly as an additional factor for consideration in differential diagnosis. He must recollect that it can mimic a host of diseases involving different organs of the body, resulting in symptoms which may cause a patient to be referred for x-ray examination of almost any region. Most of the victims of malaria can recognize its diverse manifestations and diagnose its recurrences independent of the physician. Some, however, are unaware that they have the disease or may fail to give a history of infection, and such patients can present themselves with any of the following symptoms, precipitated by fatigue, exposure, surgical procedures, and various lesser vicissitudes:

(*a*) Atypical febrile illness, resembling tuberculosis or typhoid.
(*b*) Delirium or convulsions (due to cerebral involvement).
(*c*) Abdominal pain, simulating appen-

[1] From the Department of Radiology, U. S. Naval Hospital, Oakland, California. The opinions and views set forth in this article are those of the writer and are not to be considered as reflecting the policies of the Navy Department.

Read by title at the Twenty-ninth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1–2, 1943.

dicitis, cholecystitis, and even intestinal obstruction.

(*d*) Diarrhea (malarial dysentery).

(*e*) Pulmonary disturbances, such as bronchitis and pleurisy.

(*f*) Nephritis and hematuria, including blackwater fever.

(*g*) Miscellaneous and bizarre disorders of other organs or parts of the body.

The diagnosis must be suspected in order to be made and requires the finding of Plasmodia in the blood smear for confirmation. *Plasmodium vivax* (causing benign tertian malaria) is the most widely found organism. *P. falciparum* (causing malignant tertian or subtertian malaria) is probably the most serious one. The two other and less common etiologic agents are *P. malariae* (causing quartan malaria) and *P. ovale* (causing mild tertian malaria).[2] Mixed infections may occur. Transmission is usually by one of the various species of anopheline mosquitoes.

The radiologist may be asked to examine the abdomen or urinary tract of any patient, in which event he should always note the presence of an enlarged spleen. We have seen three instances in which a correct diagnosis of malaria was first suggested by such notation, the patients being unaware of the infection or the splenomegaly. Needless to say, there are many other diseases in which splenomegaly occurs, but its presence in an obscure case should always lead to an appropriate blood study.

When may the spleen be considered to be enlarged? The spleen normally varies in size in different individuals, and from time to time in the same person; therefore, only fairly definite degrees of enlargement may be diagnosed with certainty. Despite this variation, the roentgen estimation is inevitably more accurate than the clinical, especially when uniform technical factors are adhered to. In healthy young adult males, examined supine, with a 36-inch target-film distance, the average length of the spleen shadow is 12 cm. and the average breadth 6 cm. The length is measured in a slightly diagonal fashion, from the upper to the lower pole, and the breadth at right angles to this line, in approximately the mid-part of the organ. The breadth may differ considerably from one pole to the other and must often be approximated. The length varies normally in different individuals from 8 to 16 cm. and the breadth from 4 to 9 cm. In about 15 per cent of persons the spleen shadow will be obscured or indefinite in outline; additional procedures, as fluoroscopic examination, with or without air-filling of the colon or stomach, will help in such instances. Enlargement can be diagnosed with reasonable certainty when the spleen measures *over 17 cm. in length or* (when its length is within the 12 to 16 cm. range) *over 9 cm. in breadth*. Associated roentgen findings include depression of the splenic flexure of the colon, depression of the left kidney, and elevation of the left side of the diaphragm. It is rarely necessary to resort to thorotrast lienography.

The inverted U-shaped spleen is an occasional but rare source of complexity in measurement.

We made serial examinations of the spleens in a group of cases of malaria (chiefly vivax) in males of eighteen to forty-five years, all with infections of less than two years' duration. The size of the spleen could be readily determined in 85 per cent of them and therefore we believe that the method should be used whenever exact determinations are considered necessary (Table I).

Aside from splenomegaly and, in some cases, hepatomegaly, the only notable roentgen findings reported in this disease are cerebral calcifications. These may develop in severe chronic cases, especially in falciparum malaria. They occur in the

[2] The National Research Council and the Surgeons General of the Army, Navy and Public Health Service are reported (J. A. M. A. **123:** 1052, Dec. 18, 1943) as urging the etiologic terminology for the four malaria infections of man: vivax malaria (instead of tertian or benign tertian); falciparum malaria (instead of estivo-autumnal, subtertian, malignant tertian, tropical, or pernicious malaria); malariae malaria (instead of quartan malaria); and ovale malaria.

TABLE I: X-RAY MEASUREMENTS OF SPLEEN SIZE

The figures presented here were obtained in a series of 32 cases of malaria, chiefly *vivax* infection. Measurements are recorded in centimeters, directly from films made at 36-inch target-film distance, with the subjects supine. The examinations were repeated at least once in each case, as part of an investigation conducted by Lt. Comdr. D. L. Wilbur (MC) USNR, on the effect of a certain mechanical treatment on malaria.

X-Ray Number	Size at 11 A.M.	Size at 3 P.M.*	Notes
5414	15 × 8	15 × 9	...
4473	19 × 7	19.5 × 7	May 1
4473	21 × 12	22 × 12	June 1
6287	12 × 4	11 × 5	...
6276	15 × 5	15 × 5	...
5939	25 × 6	25 × 6	...
5273	12 × 4	12 × 4	...
5254	16 × 11	16 × 10	...
5452	12 × 3	12 × 3	...
5449	12 × 3	12 × 3	...
5431	13 × 4	13 × 4.5	...
5418	10 × 4.5	10 × 4	...
5428	19 × ?	19 × ?	...
5427	11 × 5	13 × 5	...
3452	23.5 × 7	23.5 × 7	May 8
3452	23.2 × 7	23.2 × 7	May 15
2412	13 × 5	13.5 × 5	...
4618	17 × 4	16 × 5	...
4777	16.5 × 5	16 × 5	...
4673	20.5 × 6	22 × 6	May 25
4673	22 × 6	22 × 6.5	May 26
5319	14 × 7	14 × 7	...
5307	15 × 5	16 × 5	...
5303	17.5 × 6	17 × 6.5	...
5283	14.5 × 4.5	16 × 5	...
5281	23 × 7	23 × 7	...
5277	17.5 × 7	17.5 × 7	...
5157	18 × 7	19.5 × 7	...
5148	13.5 × 5.5	13.5 × 6	...
5101	21 × 5.5	21 × 5	...
2187	19 × 6	19.5 × 6	...
4976	11 × 4.5	? ?	Second film unsatisfactory
3228	17 × 6	15.5 × 6.5	...
3924	13 × 5	11.5 × 5	...
5131	18 × 7	16.5 × 6	...

* The afternoon measurements were made following a mechanical "respirator" treatment which was reported to produce, among other benefits, shrinkage of enlarged spleens. It is apparent from the above figures that no such effect took place in our cases. The "treatment" was not pursued.

hemorrhagic or granulomatous subcortical lesions (3). We made roentgen examinations of the skull in a small number of cases of cerebral malaria and in a larger group of cases of chronic malaria, none of them of over three years' duration; we did not find calcifications in any instance. Differential diagnosis would have to include the numerous other calcifying parasitic, inflammatory, and degenerative disorders of the brain.

DENGUE

Dengue may come to the attention of the radiologist because of a request for x-ray examination of the bones and joints. Patients usually show a high fever, severe pains in joints and muscles, and leukopenia. Some have, also, a rash and adenopathy. Many have pain referred to the eyeballs. The disease is due to a virus transmitted by the *Aedes* mosquito. There are no characteristic x-ray findings.

DYSENTERY

Bacillary Dysentery: This disease, due to various species of *Shigella*, is of widespread distribution and may result in serious epidemics. In the acute stage, there are no findings of specific radiological interest. In the chronic stage, x-ray changes resembling those of chronic ulcerative colitis have been reported.

Amebic Dysentery: This form of dysen-

tery, due to *Endamoeba histolytica*, is also world-wide in distribution, but is more prevalent in tropical than in temperate regions. It may be acute or chronic; carriers are common. The chronic form sometimes shows features of radiologic importance:

(*a*) Colon: Irritability and mucosal irregularities, especially in the proximal half of the large bowel, and occasional hyperplastic changes in the cecum and appendix are observed. Some believe that cecal inflammatory changes without pulmonary disease should suggest amebic colitis. Bell (4) reported conical spasm of the cecum, with segmental irritability of the colon in a group of cases.

(*b*) Liver: Enlargement of one or other lobe, with associated displacement of the colon or stomach, may be due to liver abscess. We have found this observation of gastric displacement of considerable value in two cases of amebic abscess of the left lobe of the liver. These abscesses may be single or multiple and sometimes attain enormous size. Thorotrast hepatography may help in their localization.

(*c*) Lung: Abscess of the lung, silent or otherwise, may occur, often by extension from a liver abscess. There are no pathognomonic x-ray findings.

(*d*) Miscellaneous: Abscesses of the brain and other viscera are occasionally seen.

TYPHUS AND OTHER RICKETTSIAL DISEASES

The rickettsial diseases, while of considerable clinical importance, present no roentgen findings of immediate interest, with the possible exception of Q fever. In that disease, due to *Rickettsia diaporica* or *burneti*, a patchy type of bronchopneumonia, confined to one lobe, has been reported.

Scrub typhus or tsutsugamushi disease is often followed by myocardial disturbances. We are at the present time making cardiac roentgen studies on a series of patients convalescent from this disease, and hope to report these (along with the results of kymographic observations) in a subsequent publication.

CHOLERA, YELLOW FEVER, PLAGUE, AND THE RELAPSING FEVERS

Cholera, yellow fever, plague, and the relapsing fevers have no features of outstanding radiologic interest. The pneumonic type of plague is rare and usually too fulminating to permit or require x-ray studies.

LEPTOSPIROSES

The most important of the leptospiroses is Weil's disease, due to *Leptospira icterohaemorrhagiae*. Jaundice and hepatomegaly are seen.

HELMINTHIASIS

Helminthiasis includes a large group of disorders, many of them non-tropical in nature. Only the more important ones, which show some findings of radiologic importance, will be considered here.

Hookworm disease is usually due to *Necator americanus* or *Ankylostoma duodenale*. In the former type, small bowel changes similar to those seen in deficiency disorders have been reported (5). They may subside following vermifugation. Patients with ankylostomiasis may have symptoms of duodenal ulcer, caused by presence of numerous hooklets in the duodenal bulb, with associated duodenitis (6). The thickening of the mucous membrane, irritability, and local tenderness disappear soon after administration of a vermifuge. We have seen only one case with such findings.

Strongyloidiasis, due to *Strongyloides stercoralis*, usually results merely in diarrhea. However, changes in the small bowel suggesting regional ileitis, and in the lungs (localized infiltrates), have been reported (7).

Ascariasis is the commonest helminthic infection. The worms may be recognized in the course of a gastro-intestinal examination as radiolucent shadows, occurring especially in the jejunum. They measure from 15 to 30 cm. in length and about 6 mm. in diameter. The gastro-intestinal tract of the worm itself may be outlined with the host's barium at a twelve or twenty-four hour study. Occasionally, a

bolus of worms causes intestinal obstruction.

It is of interest to note that the actual incidence of intestinal parasitism in naval personnel returning from the Pacific theatre in the years 1942 and 1943 was quite low, according to Michael (8), who published a brief table showing the percentage distribution of the conditions at that time.

TRYPANOSOMIASIS

There are two completely different forms of trypanosomiasis, the African and the American. African trypanosomiasis, due to *Trypanosoma gambiense* or *Trypanosoma rhodesiense*, causes sleeping sickness, with its associated hepatosplenic enlargement. American trypanosomiasis, due to *Trypanosoma cruzi*, causes Chagas' disease, with acute or chronic cardiac disturbances. The African type constitutes, of course, the greater health problem. No important or characteristic x-ray changes have been reported.

LEISHMANIASIS

Leishmaniasis, due to a minute parasite, *Leishmania*, may be predominantly visceral or cutaneous. The former type, or kala-azar, is characterized by fever, anemia, and hepatosplenic enlargement. It may be mistaken for malaria. Its complications are numerous and frequently severe: they include pulmonary, intestinal, and vascular disturbances. Cutaneous leishmaniasis appears in two forms: the oriental and the American. Both show ulcerating granulomas of the skin, especially of the face and upper extremities. The American type, or espundia, shows mucosal lesions as well. It is common in South America.

FILARIASIS

Three different forms of filariasis are seen in man, the most important being that due to the minute worm formerly known as *Filaria bancrofti* but now by the cumbersome title *Wuchereria bancrofti*. This is the most widely distributed of the filarial diseases, being spread by various types of mosquito, notably of the genus *Culex*.

Filariasis. Filariasis due to *Wuchereria bancrofti* and to *W. malayi* is of considerable interest to radiologists, both from the point of view of diagnosis and treatment. The incubation period varies from three to more than twelve months. In otherwise healthy adult white males, not subject to heavy or repeated infection, it may present few or no clinical symptoms. When symptoms are present, they usually consist of periodic attacks of superficial lymphangitis involving an arm or leg, with variable degrees of lymphadenitis. The lymphangitis is frequently "retrograde," extending distally from the point of initial development. Attacks of funiculitis, epididymitis, and orchitis commonly occur. Hydrocele or scrotal edema may develop. These attacks of lymphangitis may be mild or very painful. They usually subside in a week or two and may not recur for months or years. Some cases show repeated recurrences at short intervals. Edema, wheals, and other allergic phenomena occur.

After several attacks of lymphangitis, persistent edema and fibrosis may develop and the condition of elephantiasis appear. This usually takes several years and seems to occur chiefly in those with prolonged exposure, massive infection, or complicating pyogenic infection. In the late stages, chyluria, chylous ascites, and chylous diarrhea may occur. Chyluria (probably better known as lymphuria) is due to rupture of dilated blocked lymphatics into the renal pelves or ureters. If blood vessels rupture along with the lymphatics, hematolymphuria results. Some patients show no symptoms; others experience weakness, abdominal pain, and depression. The deformity of the renal pelves produced by the dilated lymphatics has been correctly diagnosed by urography.

In some patients the worms die and become calcified, producing small opacities, especially in the subcutaneous tissues, lymph nodes, and the scrotal lymphatics. These appear as small linear or dot-like shadows from 1 to 4 mm. in length and only about 1 mm. in diameter. Some observers have reported opacities up to 12

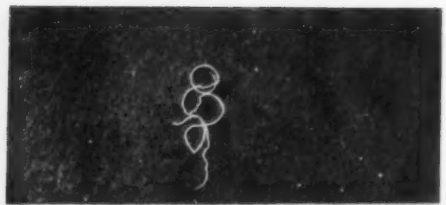

Fig. 1. *Wuchereria bancrofti* (female) from a case of filariasis in a male of twenty-six who had an infestation of about eighteen months' duration. Worm photographed in a Petri dish containing normal saline. Recovered from an enlarged left inguinal node, which was incised and placed in warm saline solution for about forty-eight hours; at the end of that time the worm had wriggled free of the node. Clinical symptoms were intermittent painful lymphangitis in left arm and left leg, and funiculitis. Courtesy of Lt. Comdr. D. L. Wilbur.

mm. in length (9). They are often difficult to recognize but are fairly characteristic, having a different distribution than calcified *Trichinae*, and being much smaller than *Cysticerci* (10). We have made roentgenograms of the extremities and scrotal areas in over fifty cases of filariasis in white adult males, all with infections of less than two years' duration, without succeeding in demonstrating calcified worms in any one of them. The worms are said to live from one to seven years and in our cases probably few were adequately calcified, even if dead, in the short time elapsing since infection. The female worm measures up to 6 cm. in length and 0.25 mm. in thickness; the male is about half that size. They are often found coiled up in a node and occasionally in a thickened lymphatic. They have been recovered alive from excised nodes, by immersion of the node in warm saline for a day or two (Fig. 1).

It is to be noted that the outstanding symptom and sign of filariasis is lymphangitis, and that the microfilariae are rarely discovered in the blood in the early stages of the disease, at least in current cases of *W. bancrofti* infestation arriving from the South Pacific area. Diagnostic skin tests are under investigation, but no really satisfactory test has yet been reported. Some authorities regard biopsy of involved nodes as inadvisable because of a tendency to initiate recurrences. A reliable skin test may therefore be all the more desirable.

In those patients who have significant pain, soreness, or other disability associated with the attacks of lymphangitis or lymphadenitis, considerable palliation and even actual arrest of an attack can often be obtained by irradiation of the involved areas. We use small doses administered to wide fields (from 50 to 100 r, in air, with fields not less than 20 × 20 cm.), with moderate filtration, half-value layer equivalent to about 0.5 mm. copper. This dose is given to the involved regions every three days for about four doses. The treatment occasionally causes a temporary accentuation of symptoms for about twenty-four hours and may induce a brief abortive attack in a previously quiescent area.

Others (11, 12, 13) have also reported favorable results in the treatment of this condition by radiation. Burhans and Camp (11) used doses of about 75 r repeated every second day for three doses; they reported that recurrences were fewer in the treated areas and that many of their patients were able to resume sustained physical work, though such efforts prior to x-ray treatment invariably induced recurrences.

Golden and O'Connor (12) reviewed the literature on the x-ray treatment of filariasis up to 1934 and also reported a group of their own cases. They made some interesting histological observations on worm-containing tissues excised subsequent to irradiation. In these "the appearance of the dead calcifying worms was quite different from that of similar worms in unirradiated tissue; giant cells in the vicinity of the irradiated worms were much more numerous, calcification of the parasites was in many instances limited to the cuticle instead of extending through them, fibrosis around them was composed of younger cell forms and was surrounded by areas of marked round cell infiltration, whereas under ordinary conditions the fibrous tissue includes areas of hyalinisa-

tion and the round cell infiltration is relatively slight."

Commenting on the results of treatment, Golden and O'Connor observed that appraisal is difficult (*a*) because attacks of lymphangitis often subside spontaneously for no obvious reasons, even under unfavorable circumstances, and (*b*) attacks which were once frequent may spontaneously become very infrequent, not recurring for several years, without any treatment. In our own experience, about 75 per cent of cases showed benefit from x-ray treatment, some of the most spectacular results being in those with very painful attacks. We would not, however, claim cure or permanent arrest in any.

Yamaguchi (13) has reported successful results in treating filariasis with total-body irradiation. He gave courses of from 11 to 22 treatments and believed that he depressed the reproductive mechanism of the worms. He also noted immediate reduction in lymphatic induration and swelling. We have not used total body irradiation in any cases.

The late complications of the disease, such as lymphuria, have also been treated with apparently excellent results. Golden (12) reported a group of cases of chyluria treated by irradiation of the kidneys. He used doses of 50 to 75 r weekly for four to fifteen doses, usually with a rest of a month or two after four doses had been given. The usual technical factors (200 kv., filter of 0.5 mm. copper and fields 20 × 20 cm.) were employed. The cases were followed for one to three years; in all of the 7 treated, the chyluria ceased during treatment; 4 patients remained well for periods as long as three years; there were 2 recurrences and one death from accidental causes soon after treatment terminated.

Onchocerciasis and *Loiasis* are two types of filariasis less common than the above. Onchocerciasis is due to *Onchocerca volvulus* (the blinding filaria). Patients show tender subcutaneous nodules, especially on the head, and sometimes keratitis and blindness. An itching lichenoid dermatitis may develop. The condition is seen in West Africa and Central and South America. Loiasis is due to *Filaria loa loa*. The patients have subcutaneous swellings, and the parasite may migrate to the subconjunctival tissues. It is to be noted that the "blinding" filaria causes intrinsic eye changes due to migration of microfilariae into the eye structures, while the *Loa loa* merely causes temporary inconvenience (when the worm passes across the subconjunctival tissues—a rather striking episode, well recorded in colored motion pictures).

Fig. 2. Dracontiasis. Calcified guinea-worm (*Dracunculus medinensis*) in the leg of an adult male. In other sites, such as the thoracic wall, the worm may be coiled up and appear as a localized calcific opacity. From Beal (14).

Dracontiasis is due to *Dracunculus medinensis*, the guinea-worm, formerly classified as *Filaria medinensis*, and for that reason considered in this section. The male worm is about 2 cm. in length, and the female from 15 to 100 cm.! Each measures from 1 to 2 mm. in diameter. They may produce no symptoms until the skin over them is punctured, usually at the

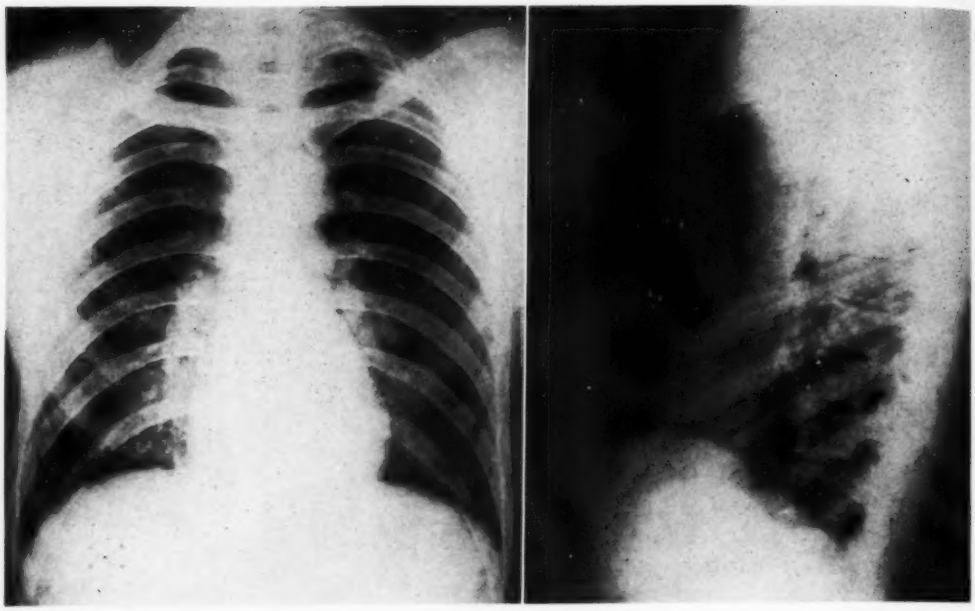

Fig. 3. Paragonimiasis (pulmonary distomiasis due to *Paragonimus westermani*). Accentuation of the basal pulmonary markings (? pneumonitis), especially on the right side. The patient was a male, aged twenty-four, with hemoptysis, cough, weakness, and pain in the lower chest for about six months. Symptoms developed after four months of jungle training in British Samoa. Sputum negative for acid-fast organisms and positive for ova of *P. westermani*. Patient also had pain in the left leg and groin with transitory cutaneous ulcers. Roentgen examination of the bones and soft tissues of these areas was negative. The clinical course was one of slow improvement.

point of emergence of the head. If retained after it dies, the worm often calcifies and appears as a segmented, linear, or coiled shadow. Beal (14) and others have reported the occurrence of these calcified worms in the leg, chest, and abdomen. Their large size renders them readily recognizable, their favorite location being in the subcutaneous tissues of the leg (Fig. 2). Castay (15) has reported them in the scrotum, the posterior thoracic wall, and the left supraclavicular region: in the first two areas they produced changes resembling cold abscesses.

DISTOMIASIS

The diseases grouped under the heading distomiasis are due to trematodes or flukes. *Intestinal distomiasis* is due to a variety of trematodes, especially *Fasciolopsis buski*. In cases of this latter type, edema may supervene on prolonged diarrhea.

Hepatic distomiasis is due commonly to *Clonorchis sinensis*. Liver enlargement, jaundice, etc., are seen.

Pulmonary distomiasis is due to *Paragonimus westermani*. The worm is actually found in many of the organs besides the lung, but pulmonary symptoms tend to predominate. Ova may be recovered from both sputa and excreta: they are small, brown, and operculated (measuring from 65 to 100 microns in length). The fluke itself measures about 8 mm. in length and 2 mm. in thickness. In chronic cases it causes small cystic lesions in the lungs, with associated inflammation and ulceration. Roentgenograms may reveal nodular thickening of the pulmonary markings, especially in the lower lobes, with variable degrees of bronchiectasis and even cavitation. The concomitant blood spitting gives rise to the term "endemic hemoptysis." Undoubtedly a better term is *paragonimiasis* (16). Four clinical types are recognized: (1) a generalized lympho-

nodular type, with fever, adenopathy, and cutaneous ulceration; (2) a pulmonary type, with cough, chest pain, bloody or purulent sputum, and variable roentgen changes in the lungs; (3) an abdominal type, with pain, tenderness, variable degrees of diarrhea, hepatomegaly, and other findings; (4) a cerebral type, with various convulsive, paretic, or other manifestations. It is reported that in some sections of Japan, cerebral paragonimiasis is included in the routine differential diagnosis of cases of epilepsy.

We have seen 8 cases of pulmonary paragonimiasis in personnel returning from the South Pacific area and have made complete roentgen examinations of the lungs in all of them. Only 2 showed significant degrees of nodular thickening of the basal pulmonary markings, bilaterally. The findings were not in the least diagnostic *per se*, but in conjunction with the history of intermittent cough and hemoptysis plus appropriate exposure, they were of some value in diagnosis (Fig. 3). In all 8 cases, the eggs were found in the sputa. None showed gross bronchiectasis, nor were the "shadows of the fluke" ever visible in any of the films. Miller and Wilbur (17) have described in detail the clinical features of 3 of these cases and are responsible for bringing our attention to this unusual condition. In two of their patients severe and persistent thrombophlebitis of the legs was present. In none were cerebral symptoms prominent.

Schistosomiasis is due to a group of blood flukes. Three types are seen in man: bilharziasis or endemic hematuria, due to *Schistosoma hematobium;* rectal or intestinal bilharziasis, due to *S. mansoni;* oriental schistosomiasis, due to *S. japonicum* (with which type liver symptoms predominate).

In infested countries, a high percentage of the population is afflicted with bilharzia (native involvement running up to 60 per cent). The mode of infection is through an abrasion in the skin. All organs of the body are affected, the genito-urinary and gastro-intestinal tracts being the most commonly and most severely involved. The clinical diagnosis is said to be simple, the principal symptom being bleeding from the urinary or gastro-intestinal tract. The diagnosis is confirmed by finding the ova in the excreta. The ova are deposited in the submucosa, giving rise to ulceration and subsequent calcification, which can be shown roentgenographically. Two forms of reaction are seen: calcific streaks in the walls of involved areas; oval densities like stones or calcified papillomata.

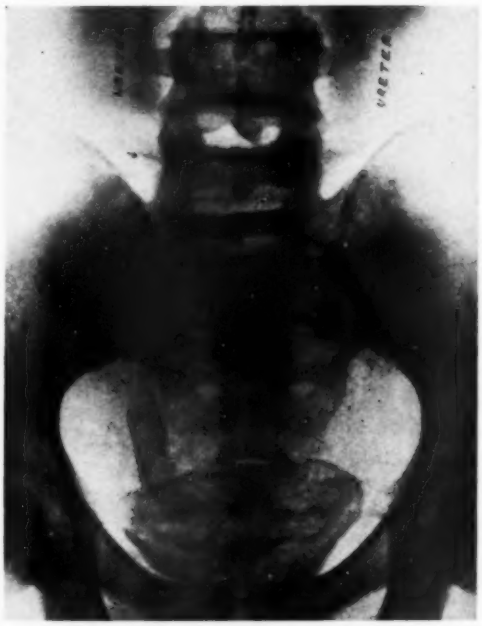

Fig. 4. Bilharziasis. Calcified ova in submucosal tissues of bladder and ureters, in an adult male with urinary bilharziasis, due to *Schistosoma hematobium*. Note the faint calcific streaks in portions of the ureteral walls. From Ragheb (18).

The first form is predominant in the bladder and ureters. The second form is found commonly in the intestines and the kidneys. Papillomas in the intestinal tract are not usually calcified, except in the region of the appendix. Those occurring in the kidneys are usually calcified, causing shadows which resemble stones. The calcifications in the urinary tract are fixed in position and may not increase in size even in the course of years. They do not en-

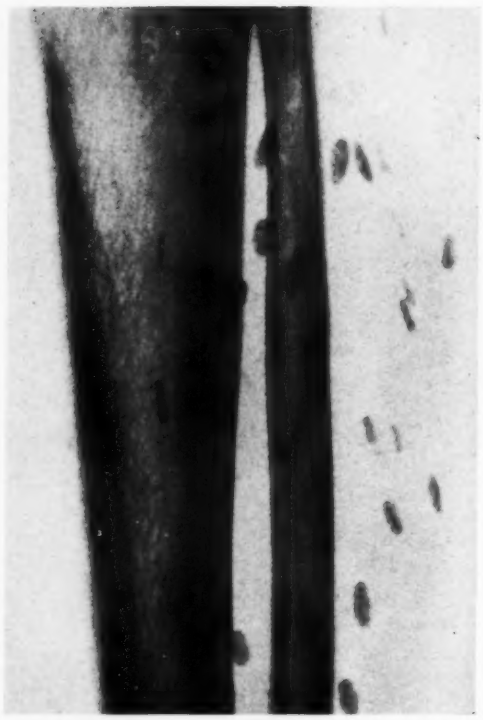

Fig. 5. Cysticercosis. Calcified cysticerci in the skeletal muscles of a male, aged thirty-eight. This patient also had calcified cysts in the soft tissues of the neck, the thoracic wall and the abdomen. His approximate date of infestation was fifteen years previously. Autopsy proof. *Note:* The calcified cysticerci often vary greatly in shape and size. They may be oval, circular or triangular in shape, from 0.2 to 5 mm. in diameter, and from 0.2 to 20 mm. in length. In the brain they tend to be small and spotty (from 1 to 3 mm. in diameter). From Brailsford (21).

croach on the lumen, as they are embedded in the mucosa. The calcified papillomas are readily seen roentgenographically, the uncalcified ones by the aid of opaque media. The bladder (Fig. 4) is usually the first organ to show evidence of disease (18).

Cases of pulmonary nodulation, due to ova or adult worms reaching the lungs, and resembling miliary tuberculosis, have been reported in both the urinary (*S. hematobium*), and the intestinal (*S. mansoni*) forms of the disease (19, 20).

TENIASIS

This group of diseases is due to cestodes or tapeworms.

Diphyllobothrium latum, the broad tapeworm, causes few serious symptoms except anemia. It measures from 2 to 10 meters in length.

Taenia solium, the pork tapeworm, causes variable symptoms, usually mild. It measures about 2.5 cm. long. Its larval form, *Cysticercus cellulosae*, causes *cysticercosis*. Cysticercosis is usually acquired by eating "measly" pork and may be associated with serious symptoms. The larvae may occur in any organ in the body, but especially in the brain and eye, and symptoms vary accordingly. In the brain, they may cause epilepsy; in the eye, visual aberration; in the muscles, rheumatism, etc. When calcified, which rarely occurs until at least five years after infestation, the larvae become visible on roentgenograms. In the brain they show as small opacities, 1–3 mm. in diameter, scattered through the substance of the organ. In the muscles (where they are much more apt to become calcified than in the brain) they usually appear as ovoid densities, about 2 × 10 mm., lying in the direction of the muscle fibers (Fig. 5). They range in number from one to several thousand in a single patient, and may vary greatly in size and shape (21, 22). In the differential diagnosis of brain lesions, tuberous sclerosis may be considered but does not show any associated skeletal muscle calcifications. There are other unusual inflammatory and degenerative cerebral conditions in which patchy calcification occurs, but space does not permit their consideration here. In the differential diagnosis of muscle calcification there is usually little difficulty: in trichinosis the calcified areas are only about 1 mm. in diameter; in calcinosis interstitialis they are usually linear and diffuse.

Taenia saginata, the beef tapeworm, occurs in man only in adult form and is not associated with any specific findings of immediate interest.

Taenia echinococcus (now know as *Echinococcus granulosus*), the dog tapeworm, occurs in man only in its larval form, causing hydatid disease or *echinococcosis*.

While not strictly speaking a tropical disease, this condition occurs sufficiently often in persons returning from overseas (especially Australia and Iceland) to be worth considering here. The echinococcus or hydatid cyst is formed by liquefaction of the larva after it has invaded the tissues. It grows slowly and its wall is composed of two layers, an external laminated cuticle and an internal germinative layer, a fact of diagnostic value in some pulmonary hydatids (23). The cysts may be simple or complex; some are sterile; some become secondarily infected. They may rupture into hollow viscera, such as bronchi, intestinal tract, biliary tree, and urinary tract.

Hydatid cysts occur most frequently in the liver (over 50 per cent of cases.) They also occur in the lungs, pleura, abdominal viscera, bones and, rarely, in the nervous and cardiovascular systems. Some are small and symptomless; others are large and produce serious symptoms. In solid viscera, such as the liver, cysts tend to undergo calcification of their walls, while in non-resistant organs, such as the lungs, they rarely or never do so. In bone, a patchy cystic appearance develops, resembling fibrocystic disease or osteolytic metastatic carcinoma; the ribs and pelvis are common sites. In the brain the diagnosis has been made by aspiration and air filling. In the lungs, well defined circular opacities occur; they may be quite large but usually vary from 3 to 8 cm. in diameter. Bone and lung lesions may coexist.

TROPICAL TREPONEMATOSES

The tropical treponematoses include yaws, pinta, and bejel, all granulomatous diseases due to treponemata, and rarely seen in this country. In the chronic or late stages, lesions of bones and viscera may occur, similar to those seen in syphilis. We have seen one case of *yaws* in an officer who accidentally infected a finger while in the South Pacific area. He developed a nodular granuloma at the site of inoculation, with regional adenopathy and a rash; *Treponema pertenue* was found on dark-field study. The lesion regressed promptly with bismuth treatment. In some endemic areas, peculiar tertiary forms of yaws are seen: (*a*) goundou, a chronic sclerosing osteoperiostitis of the superior maxillae, and (*b*) gangosa, a destructive ulcerating process of the nose and palate, especially of the cartilaginous portions. Gangosa may also be due in rare instances to cutaneous leishmaniasis. The x-ray appearance of such advanced lesions is readily visualized.

Pinta, due to *Treponema carabeum*, is seen in Cuba, Mexico, and Central and South America. It may result in various visceral lesions similar to those of tertiary syphilis, including aortic aneurysm. There are no characteristic roentgen findings.

TOXOPLASMOSIS

In toxoplasmosis, a rare condition due to a sporozoan, the *Toxoplasma* (probably of the Haemosporidia group), various cerebral and pulmonary lesions of radiological interest have been reported. In infantile toxoplasmosis diffuse cerebral calcifications may occur, in association with symptoms of encephalomyelitis. The calcifications are usually bilateral, vary from 1 to 3 mm. in diameter, and are located in the cerebral hemispheres; curvilinear streaks may be present in the basal ganglia. Areas of demineralization in the diaphyseal ends of the long bones and of pneumonitis in the lungs have been noted. In adult toxoplasma infections, bilateral pulmonary infiltration, of a type similar to that occurring in influenzal pneumonia, may be seen. Lesions of the heart muscle and skeletal muscles (presumably granulomatous infiltrates) are also reported.

LEPROSY

Leprosy is largely of academic interest in this country. It is to be remembered, however, that in cases of the neural type, various degrees of concentric atrophy of the phalanges and small bones of the hands and feet are seen. This concentric atrophy may result in spontaneous amputations

and other deformities (24). These are not entirely diagnostic, however, since similar findings are present in some other neurotrophic disorders and in certain peripheral vascular diseases. Rarely, true leprous granulomata occur in the bones; these produce the same roentgen changes as other granulomata.

MISCELLANEOUS LESIONS

Tropical Ulcers: Various types of tropical ulcers (sloughing phagedena) may be encountered, especially of the feet, hands, and face. These are commonly due to spirochetal and bacillary organisms. They often extend to adjacent bones and joints. X-ray changes are those of a severe infectious osteitis or osteoarthritis. In recent months there have been reports of pathogenic diphtheria bacilli being found in some tropical ulcers and desert sores. These have occasionally been virulent and associated with characteristic paralyses and other symptoms.

Ainhum is clinically equivalent to spontaneous amputation of the little toe; it is apparently a neurotrophic disorder. Films show atrophy or disappearance of the phalanges.

Madura foot, or mycetoma, is a fungus infection, usually involving the foot and resulting in chronic swelling, ulceration, and sinus formation. The bones and joints show varying degrees of destruction and osteoporosis.

Acne vulgaris and Epidermophytosis. These quite non-tropical disorders show a tendency to special and severe types of exacerbation under some tropical conditions. Since x-ray treatment is often an important factor in their alleviation or cure, they are mentioned here. They are a prolific source of hospitalization of otherwise healthy young men. Many cases respond promptly to small doses of roentgen radiation (50–150 r), repeated weekly for four to eight weeks.

SUMMARY

Some tropical diseases of importance to the radiological consultant are reviewed. The pleomorphic symptoms exhibited by many of them are stressed.

Two aphorisms well known to clinicians are repeated: "In any person returned from the tropics who becomes ill, suspect malaria" *and* "Before a disease can be diagnosed, it must be thought of."

The principal diagnostic features of some tropical diseases include findings of considerable radiological importance. In the treatment of a few of them, the judicious use of irradiation is of value.

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Osteoporosis Circumscripta Cranii: Its Pathogenesis and Occurrence in Leontiasis Ossea and in Hyperparathyroidism[1]

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THE PATHOGENESIS and classification of the large, irregular, circumscribed areas of osteoporosis of the cranium first described by Schüller[2] were for some time subjects of mere speculation. Schüller (14, 15) himself did not originally point out the intrinsic significance of his striking radiological findings. Soon, however, Sosman (17, 18) provided histologic observations indicating a relationship between osteoporosis circumscripta and Paget's disease. Further clinical and radiological investigation seemed to corroborate this evidence to a great extent, and osteoporosis came to be generally considered as an atypical form or precursor of Paget's disease, "probably the absorptive or destructive phase with the productive phase held in abeyance" (17). Its occurrence solely in the skulls of persons suffering from Paget's disease was thought to be related chiefly to the peculiarities of the diploic circulation, the cranial architecture, and the statics of the bones of the cranium (6).

Subsequent histologic studies, however, did not unanimously support the view that circumscribed osteoporosis is without exception an early or atypical form of Paget's disease of the skull. While a group of observers (2, 16, 20) microscopically verified the identity of the two conditions in four cases, Schmorl's (13) interpretations were different. In the skulls of five persons who had been suffering from Paget's disease he saw gross as well as microscopic departures, which he identified as the results of circulatory disturbances. They seemed to resemble hemorrhagic infarctions rather than the anatomical changes characteristic of Paget's disease. In gross appearance they corresponded to the fundamentals of osteoporosis circumscripta. A similar observation was made by the present writer (20). In a verified case (Case II) of osteoporosis he saw discolored areas of deep reddish hue in the cranium, which revealed microscopically an unusual hyperemia, small hemorrhages into the bone marrow, and advanced decalcification of the bone tissue, but no signs of Paget's disease. A third group of pathological findings, reported by Schellenberg (12), and later Guillain, Ledoux-Lebard, and Lereboullet (3), bore more resemblance to osteitis fibrosa than to Paget's disease.

A review of the literature shows that clinically about 60 per cent of the published cases of osteoporosis circumscripta have been associated with Paget's disease; 20 per cent, however, were connected with leontiasis ossea or bony tumors of the maxilla and not with Paget's disease. In the remaining 20 per cent the skull only was examined and not the entire skeleton; consequently, no statement can be made concerning the presence or absence of Paget's disease in these patients.

It seems, therefore, that leontiasis ossea constitutes the second largest group of abnormalities in which osteoporosis circumscripta occurs, and the coincidence of these conditions is so frequent as to have definite significance. Yet this association did not substantially increase our knowledge of osteoporosis, nor did it change our conception of its pathogenesis, despite repeated attempts (1, 6) to emphasize the connection between the two conditions. This failure to influence opinion concerning the causative relation between osteoporosis and Paget's disease may be due to the confusion in the identification of leon-

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[2] Kasabach and Gutman (6) called attention recently to the fact that Sherwood Moore (10) observed osteoporosis circumscripta in a case of Paget's disease in 1923. Moore later confirmed this statement (11).

tiasis ossea itself. In one of the cases reported by Kasabach and Gutman (6), for instance, in which osteoporosis was associated with a condition believed to be leontiasis ossea, the latter was variously interpreted as leontiasis ossea, Paget's disease, osteitis fibrosa, osteofibroma, and osteoma. In fact, it is not until recent years that progress has been made in the differentiation and classification of the various types of this rare disease (7, 19). It is thought today that probably more than a third of the cases described and published as leontiasis ossea were in fact Paget's disease, while another large group was found to be osteitis fibrosa cystica (type von Recklinghausen). The true form, called type Virchow, proved to be the rarest of all conditions published under the denomination of leontiasis ossea. It is not unlikely, therefore, that in some cases in which osteoporosis was associated with a disease considered to be leontiasis ossea we were in reality confronted with Paget's disease. This may be the reason why so little consideration was given to those remarkable observations which might have changed our concept of the pathogenesis of osteoporosis circumscripta.

Recently, the author had the opportunity to observe the occurrence of osteoporosis circumscripta in a case of histologically verified leontiasis ossea (type Virchow).

CASE I: A 63-year-old white woman had been suffering since 1921 from repeated dental infections and from sinus trouble. At that time x-ray examination supposedly revealed that parts of the bone of the upper jaw were "filling in." In 1931 the patient noticed that her right cheek bone was becoming more prominent. In 1934 her upper gum began to grow thicker and the left cheek began to protrude. Several sinus operations were performed and a number of teeth were extracted. Each instrumentation seemed to the patient to aggravate the condition and to increase the size of the maxilla. On admission (1944) the cheek bones, especially the area of the zygoma, on both sides, were prominent. The eyes lay deep in the facial bones. The gums were thickened up to 2 cm., covering almost entirely the few remaining teeth. The face was stiff, moving but little when the patient spoke and having a mask-like appearance (Fig. 1). There was no tenderness over any part of the face and the percussion note over the cranial vault was not abnormal. There was present a smooth elevation in the right parietal area, protruding a few millimeters above the level of the bone.

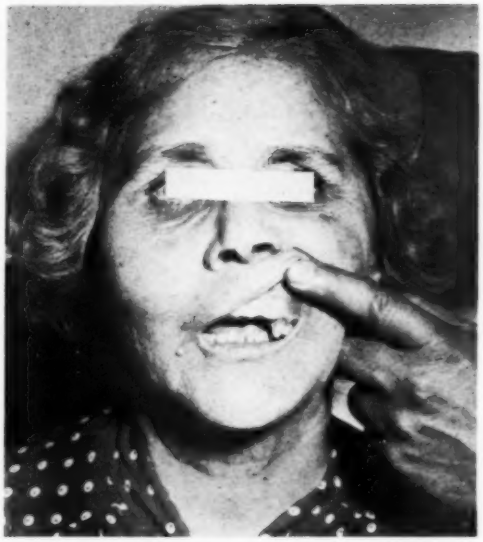


Fig. 1. Case I: Portrait of patient with leontiasis ossea, showing protrusion of maxillary areas on both sides and greatly thickened gums.

Other findings were of no significance. No impairment of vision or hearing was noted, and no abnormalities of the extremities were observed. No evidence of Paget's disease was discovered in any part of the skeleton.

The Wassermann reaction was negative. The blood count was within normal limits. Blood chemistry (followed up for three months): calcium 13.5–7 mg.; phosphorus 4.0–7.0 mg. per 100 c.c. of serum; phosphatase activity 8–12 Bodansky units.

The x-ray examination revealed an extensive thickening of almost all the bones of the face, resulting in a marked protrusion of the zygomatic regions and of the anterior walls of both maxillary sinuses. The lateral wall of the antrum and the alveolar process on both sides were remarkably thickened, relatively translucent, revealing, however, some denser areas in the vicinity of the remaining teeth. The nasal cavity, too, was narrow, and all the sinuses were obscured. The bones of the base of the skull were not visibly changed. The sphenoid sinus was small and partly filled out by bone (Fig. 2).

The skull was symmetrical; the thickness of the vault measured about 7 mm. The sutures were obliterated. The inner table was smooth. There was a large irregular defect involving the right half of the frontal bone and parts of the parietal and occipital bones on the right. It was irregularly bounded and went through the obliterated sutures

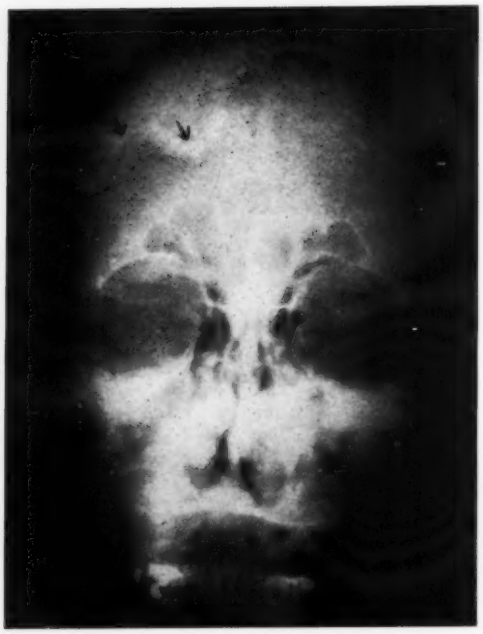


Fig. 2. Case I: Postero-anterior view of the skull, showing considerable thickening and sclerosis of the maxilla and of the malar bones. Partial obliteration of the maxillary sinuses and of the nasal cavity. Osteoporosis circumscripta indicated by arrows.

without changing its outlines. In the area of the defect both the internal and external table had become thinner, and almost the entire thickness of the bone was formed by the diploe. This contained little calcium and consequently a large defect was observed in the roentgenograms of the vault (Fig. 3).

The skeleton was carefully studied fluoroscopically; roentgenograms were made of the spine, pelvis, and lower extremities and no abnormalities were discovered.

On Jan. 6, 1944, a biopsy was done in the area of the alveolar process of the right maxillary second incisor and cuspid. The patient believed that this area was steadily getting thicker. The surgeon noticed that the bone was remarkably soft. The specimen obtained was dark red, and fine bone spicules were palpated in the rough cut surface.

Histologic examination (Figs. 4–5), of which we shall publish a more detailed record later, showed the normal bone structure to be replaced by irregularly distributed bone lamellae embedded in fibrous marrow. The structure of the lamellae consisted of a system of haversian canals with many lamellae parallel to the surface. The bone cells were small but of regular proportion and outline and evenly distributed. No signs of mosaic structure or of dark connecting lines could be discerned. Signs of intense new formation of bone lamellae were present. Frequently the surface of the spicules was surrounded by a layer of osteoblasts and in other parts of the specimen by osteoid layers. Osteoid tissue was also seen in the fibrous marrow. A number of giant cells of osteoclast type were lying in Howship's lacunae. Newly formed bone lamellae were sometimes found in the vicinity of quiescent bone structures without osteoblasts or osteoclasts on their surface. The connective tissue replacing the bone marrow contained some inflammatory cells, some psammoma bodies, and relatively few capillary blood vessels. Additional findings were irregular areas of complete bone resorption (Fig. 6). The latter did not contain bone tissue, marrow, or blood vessels, but were filled out by fine granular eosinophilic material.

The histologic diagnosis was, therefore, as follows: "Complete transformation of the bone tissue with hyperplasia due to osteoblast activity and simple metaplasia; fibrous bone marrow containing inflammatory cells and capillary blood vessels; bone resorption by osteoclasts with formation of small cavities." There were no changes present suggesting Paget's disease.

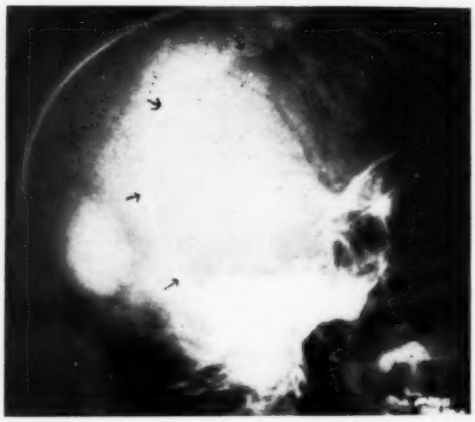
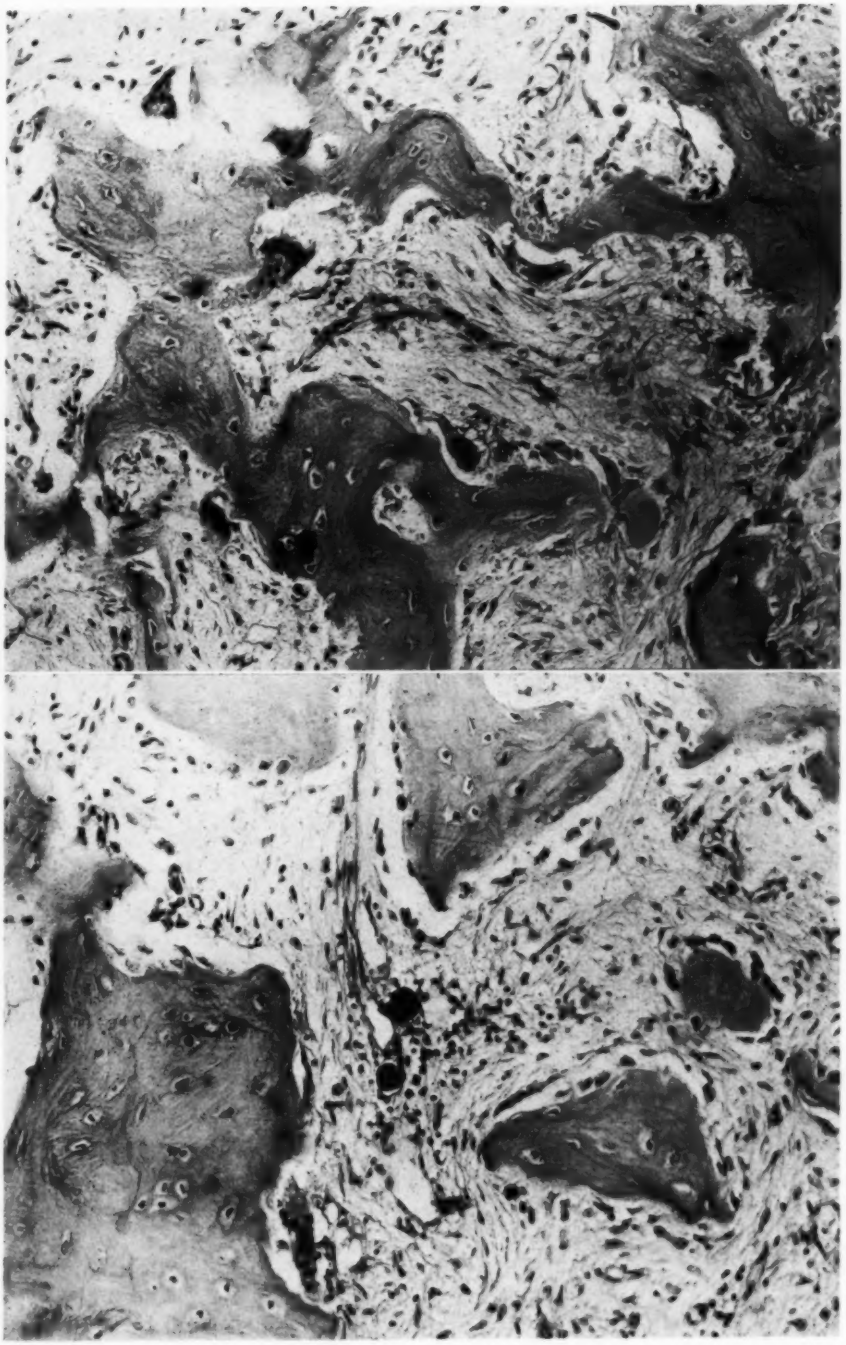


Fig. 3. Case I: Lateral view of the skull. Boundaries of the osteoporosis circumscripta indicated by arrows. Circumscribed density in occiput corresponds to the palpated elevation on the skull.

Comment: The possibility of Paget's disease in this case was excluded by clinical, radiologic, and histologic investigation. Had leontiasis ossea invaded the cranium, as might have occurred, then bony hyperplasias or hyperostoses would have resulted instead of osteoporosis. We have, consequently, to regard the osteoporosis in this particular case as secondary to leontiasis ossea but not intimately and topically connected with it.



Figs. 4 and 5. Case I: Photomicrographs of biopsy specimen from the gum, showing fibrous marrow; new formation of bone lamellae by osteoblast activity; osteoid tissue in the bone marrow; bone resorption by osteoclasts. The lower view shows the inflammatory cell reaction and psammoma bodies in the fibrous marrow.

Pathologically two forms of osteoporosis circumscripta are known. One represents circulatory disturbances, the other Paget's disease. Their radiologic signs are identical, and these same signs occur in the vault in cases of leontiasis ossea. Since no pathological findings other than the aforementioned ones have come to light, and as Paget's disease was excluded in our case, we have to assume that the anatomic basis of the osteoporosis circumscripta in this particular instance was hemorrhagic

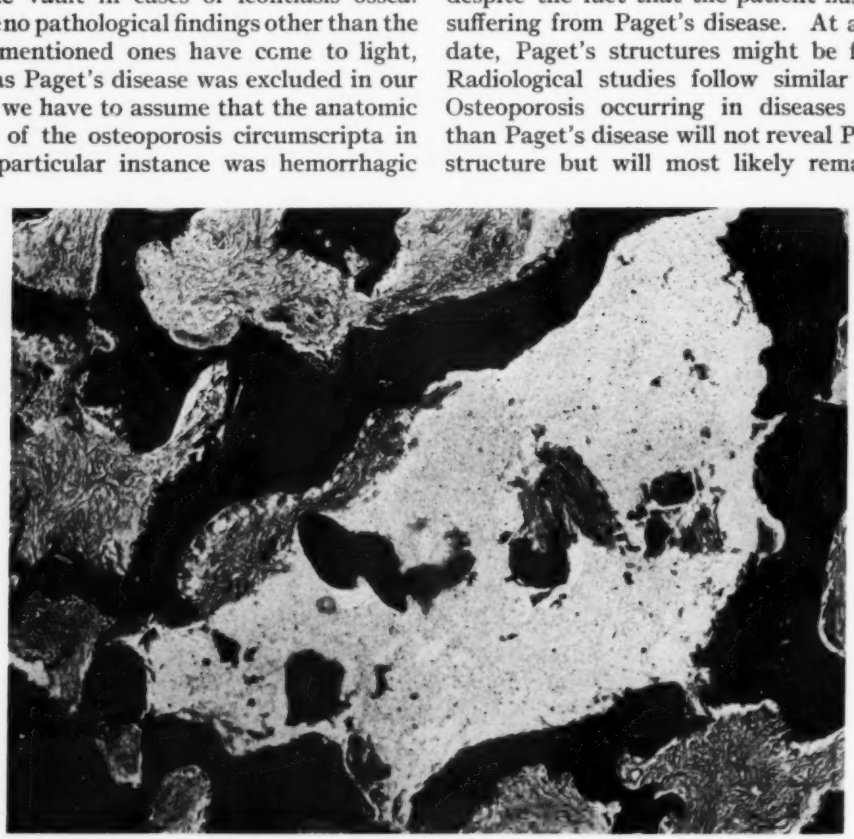


Fig. 6. Case I: Cavity of resorption with liquefaction of small areas of the bone marrow.

changes based on circulatory disturbances and decalcification of the bone tissue. We might as well assume that this form of osteoporosis is a primitive non-differentiated common reaction of the cranium which in cases of Paget's disease may be secondarily transformed into mosaic structures and fibrous bone marrow. This might happen as soon as the disturbed statics of the cranium require a bony reinforcement of the areas of the osteoporosis (sometimes even after as long a period as ten years). Consequently, if the osteoporotic lesions are investigated pathologically *before* Paget's disease is established in them, they will reveal, under the microscope, primary changes, such as hemorrhages, hyperemia, and decalcification, despite the fact that the patient has been suffering from Paget's disease. At a later date, Paget's structures might be found. Radiological studies follow similar lines. Osteoporosis occurring in diseases other than Paget's disease will not reveal Paget's structure but will most likely remain in a primitive stage, unless the leontiasis ossea or other primary bone lesion associated with its occurrence encroaches upon the osteoporotic areas. Case II is an example.

CASE II: Radiographs (Figs. 7 and 8) of a 58-year-old woman afflicted since her youth with a peculiar bone condition of the skull, called fibrous osteodystrophy, and clinically appearing as leontiasis ossea, showed extensive hyperostoses of the cranium. They were surrounded by wide areas of osteoporosis, giving the impression that the osteoporosis was not a part of the osteodystrophy but a change pri-

marily involving the vault. Hyperostoses seemed to be established in them as secondary transformations.

Another case of osteoporosis circumscripta associated with bone changes of hyperplastic type, namely with hyperparathyroidism, came to our attention a short time ago. It has occasionally been thought that some connection may exist between circumscribed cranial osteoporosis and hyperparathyroidism, though they were never found to occur together. This may be due in part to the fact that skulls

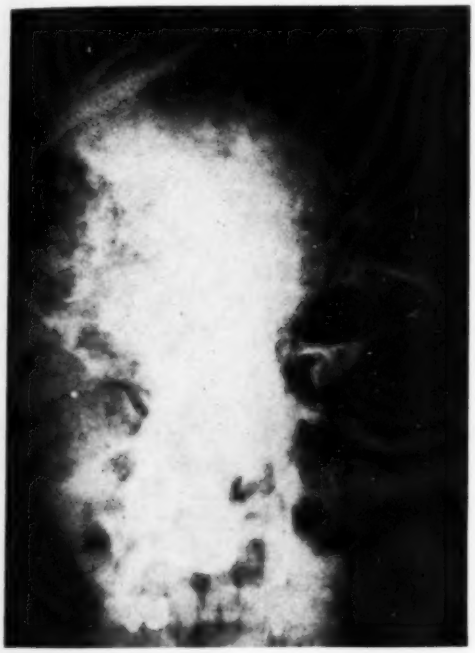


Fig. 7. Case II: Leontiasis ossea caused by osteodystrophy. Marked deformity of the face and displacement of the right orbit by hyperostoses. Obliteration of ethmoid and nasal cavities and of the right maxilla.

in hyperparathyroidism are as a whole diffusely decalcified, and an additional loss of calcium in circumscribed areas is less obvious roentgenographically than in a normal skull. The only cases in which osteoporosis was thought to be histologically related to hyperparathyroidism were those mentioned above as resembling osteitis fibrosa (3, 12). These patients were not afflicted with hyperparathyroidism,

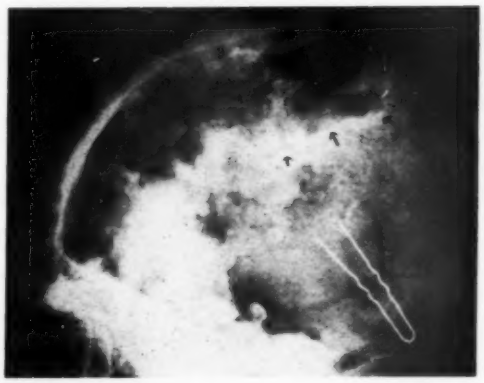


Fig. 8. Case II: Large areas of osteoporosis surrounding hyperostoses of the calvarium. Boundaries of osteoporosis marked by arrows.

and it might be well, indeed, to assume that the interpretation of the histological findings as osteitis fibrosa represents a somewhat generous use of this terminology. Kasabach and Gutman (6) found in one of their cases (No. 20) osteoporosis circumscripta of the frontal and occipital bones and Paget's disease of the tibia. Examination of the blood unexpectedly yielded values more consistent with hyperparathyroidism. A parathyroid tumor was subsequently removed. Sosman (18) made the observation that x-ray irradiation of the area of the parathyroid glands produced a reossification of osteoporotic lesions. The mechanism of the action of x-rays, however, is not quite clear for, in addition to the parathyroid glands, other structures have been irradiated at the same time.

CASE III: A third case studied by the author was that of a 56-year-old woman, who had suffered more than five years from a painful bone condition. At the same time she had a chronic kidney infection with stones. One stone had been removed in 1927. The pains in the bones and joints had increased so appreciably in the last two years that the patient became bedridden. Her ribs and pelvis were extremely tender to the touch. She was moderately anemic and all the time had an increased non-protein nitrogen in the blood.

The first roentgenograms of the skeleton were not entirely characteristic of hyperparathyroidism. They were variously interpreted as metastatic carcinosis, menopausal disturbances, and bone changes due to chronic renal deficiency. After several years

Fig. 9. Case III: Circumscribed osteoporosis in hyperparathyroid skull. Boundaries of osteoporosis marked by arrows.

of observation, however, more or less typical clinical, radiological, and biochemical evidence of hyperparathyroidism became apparent, and after a fracture of the right femur, a parathyroid adenoma was removed (Dr. Eloesser). It measured 3.5 × 2.5 × 2.8 cm. and weighed 7 gm. Histologic examination showed it to be of mixed chief and water-clear cell type. The patient's blood calcium never exceeded 12.7 mg. per 100 c.c. of serum. The phosphorus averaged between 4.6 and 5.3 mg., and the phosphatase activity was 39.3 Bodansky units. Three weeks after the removal of the tumor the phosphatase activity decreased to 12 Bodansky units. At the same time the blood calcium had a level of 6 mg. and the phosphorus 2.5 mg. per 100 c.c. of serum. Soon after operation tetany developed but was controlled by calcium medication, and the clinical condition improved temporarily.

X-ray examination of the skeleton showed the extensive changes common in advanced hyperparathyroidism. There was an extraordinary disturbance in many of the bones, consisting in diffuse osteoporosis except in the vertebral bodies, which were of increased density. Multiple cysts were seen in the innominate bones and in the upper end of each femur and in two ribs. The long bones were slightly deformed, and the trabeculation of the spongiosa was irregular. The skull was symmetrical, the calvarium up to 16 mm. thick, with granular decalcification and hyperplasia of the diploic layers. The inner and outer tables were almost indistinguishable, and a fine granular mottled diploe gave an appearance characteristic in hyperparathyroidism. There was a large circumscribed area of increased translucency involving the right frontal, parietal, and temporal bones (Fig. 9). Sharp outlines toward the posterior portions of the vault gave a distinct contrast between the structureless and consequently almost calciumless anterior areas of osteoporosis and the fine granular mottled posterior portions of the cranium. There was a wide oblique spontaneous fracture line through the occipital squama, such as occurs occasionally in cases of excessive decalcification in hyperparathyroidism.

Comment: The localization, outlines, and distribution of the osteoporotic areas in the cranium in this case of hyperparathyroidism were similar to those seen in Paget's disease and in leontiasis ossea. The osteoporosis developed about five years after the first signs of bone changes in the cranium were noticed. This corroborates our previously expressed opinion and might permit us to assume that the structural changes caused by hyperparathyroidism had possibly acted on the circulatory system of the skull in a similar way to that of hyperplasias in Paget's disease or in leontiasis ossea. Signs of rapid decalcification of the skull had been observed from the beginning. Only later, however, as the bone changes were more advanced (so as to impair the blood circulation of the calvarium), were additional areas of more profound decalcification, namely osteoporosis circumscripta, detected.

Despite the conclusive clinical, radiological and biochemical findings and the presence of the parathyroid adenoma, the early course of this case was not entirely typical of hyperparathyroidism. The vertebral bodies were remarkably dense, and the reaction of the patient to the parathyroidectomy was slight. We had to assume that a spontaneous reossification of parts of the skeleton had begun before the removal of the parathyroid tumor, as in the cases of Lindén (8), Jacobs and Bisgard (4), and others. Some balance, therefore, between the parathyroid activity and the calcium metabolism was at that time already established. This would explain, too, the development of tetany after the removal of the parathyroid tumor.

The significance of our findings of circumscribed osteoporosis in this hyperparathyroid skull remains, in spite of the above diagnostic complications, inasmuch as the radiological appearance of the skull

in hyperparathyroidism is not specifically characteristic of that disease. It occurs as a reaction of bone tissue to rapid decalcification regardless of the cause.

CONCLUSION

The coincidence of osteoporosis circumscripta (Schüller) with a proved case of leontiasis ossea (type Virchow) and its occurrence in hyperparathyroidism furnish conclusive evidence that this condition cannot be considered as a precursor or an atypical form of Paget's disease, as has been thought. It is to be regarded as a bone reaction characteristic of the structural architecture of the cranium but not indicative of a specific disease. Distinction can be made histologically between a primitive, non-differentiated form (decalcification with hyperemia and other signs of circulatory disturbances) and a secondary, differentiated form (in which proved cases were limited to Paget's disease). Radiologically, early stages of differentiation are not distinguishable from the non-differentiated form. (Later, cotton-wool structures appear in cases of Paget's disease.) It is not unlikely that occasionally encroachment into the cranial vault by leontiasis ossea is preceded by osteoporosis circumscripta (see Case II). Clinically, approximately 60 per cent of the known cases of osteoporosis circumscripta are connected with Paget's disease. Other associated conditions were leontiasis ossea, bony tumors of the jaw, hyperparathyroidism, and brain tumors.

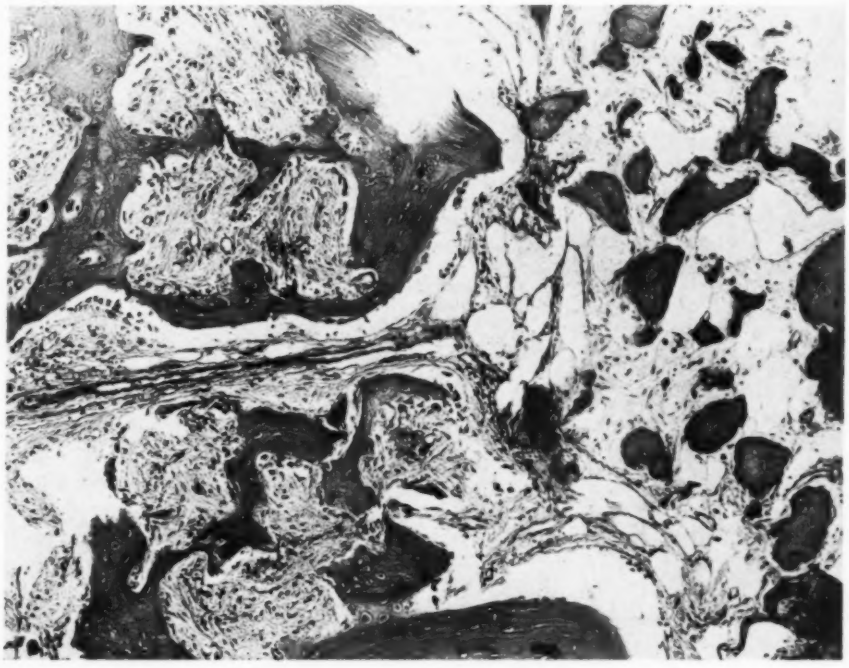


Fig. 10. Longitudinal section of an obliterated blood vessel bordering margins of quiescent and growing bone tissue (Case 1).

Concerning the pathogenesis, all findings converge on circulatory disturbances caused by space-occupying lesions near the base of the skull or in the facial bones. Statistically the bony hyperplasias of Paget's disease are most frequent. Microscopic serial examination of our biopsy specimens occasionally revealed obliterated blood vessels running into areas of quiescent bone tissue with no cellular reaction around the lamellae. The vessels

were surrounded by growing bone tissue and fibrous marrow (Fig. 10). Areas of primitive osteoporosis may undergo structural transformation corresponding to the demands or pretensions of the statics of the vault. In cases of Paget's disease mosaic structures, new formation of bone tissue, and fibrous metaplasia of the bone marrow may occur microscopically in areas of osteoporosis, furnishing the anatomical basis of the cotton-wool structures of the roentgenograms

SUMMARY

1. Osteoporosis circumscripta (Schüller) has been described in the skull of a 63-year-old woman suffering from leontiasis ossea. Histologic examination of a biopsy specimen in this case permitted us to classify the lesion as leontiasis ossea (type Virchow) and to exclude Paget's disease.

2. Osteoporosis circumscripta was observed in the skull of a 56-year-old woman with hyperparathyroidism.

3. Osteoporosis circumscripta cannot be regarded as a type of or a phase of Paget's disease or of any disease entity. It occurs most often in Paget's disease, however, and frequently may be transformed into it. The "primitive" form of osteoporosis circumscripta, described in this paper, is a characteristic reaction of the bones of the cranium and is most likely caused by circulatory disturbances in the presence of bony hyperplasias or of bony tumors near the base of the skull.

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Significant Skeletal Irregularities of the Hands[1]

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CAREFULLY conducted roentgenographic examination of the hands frequently may be as valuable a procedure to the roentgenologist as funduscopic observation is to the ophthalmologist. It is well known that the ophthalmoscope often reveals changes in the eyegrounds which denote the presence of either generalized systemic disease or a localized pathological process in some remote portion of the body. The fact that similar diagnostic potentialities are inherent in the skeletal structure of the hands and wrists has not been so fully appreciated.

Diagnostic prospecting in the form of roentgenographic skeletal survey in search of an obscure disease process is a commonly employed procedure, especially in pediatric practice. In many instances "films of the long bones" furnish the key to what has previously been a diagnostic puzzle. Unfortunately, roentgenograms of the hands are often deemed unimportant in such a survey, although, in reality, no part of the skeleton may be more revealing.

Examination of the hand is probably the simplest of all radiographic procedures, but this very simplicity tends to produce laxity on the part of the examiner, inattention to details of examination, and slipshod technical results. The sight of one or several phalanges obscured by identification markings, clipped film corners, etc., is too often the rule rather than the exception. These technical blemishes are unsightly and unnecessary. On occasion, their presence may lead to serious diagnostic errors of omission, particularly in infants and young children, in whom the metacarpals and phalanges are relatively small and notoriously difficult to position.

[1] From the Department of Roentgenology, University of Michigan, Ann Arbor, Mich. Read by title at the Twenty-ninth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1–2, 1943.

Todd's splendid monograph (1) on the maturation of the hand emphasizes in effect the desirability of good film quality and it would be of distinct value if it went no further. Greater importance lies in the fact that this monograph constitutes an excellent normal standard with which to compare the abnormal. Against this background of near perfection in normalcy, it seems justifiable to review some of the significant skeletal abnormalities of the hand, laying particular stress upon those carpal, metacarpal, and phalangeal changes which reflect the presence of disease elsewhere in the body.

ENDOCRINE DISEASES

Some of the unusual manifestations of the endocrinopathies are reflected in the hands and wrists in such a manner as to make the etiologic factor recognizable from a study of these structures alone. This is true not only of infants and children but of adults as well. For example, the roentgenographic appearance of the hands in acromegaly is so characteristic that the presence of a pituitary eosinophilic adenoma may be suspected even in the absence of intrasellar erosion. Large, broad, spadelike hands with overgrowth of the terminal phalangeal tufts, prominence of bony protuberances along the shafts of metacarpals and phalanges, and a peculiar soap-bubble pattern of distorted trabeculae in the bone ends comprise the changes commonly encountered.

Many disease entities in infancy and childhood produce delay in the time schedule of epiphyseal ossification, but none is so profound as that seen in cretinism. In addition to retarded bone age, the untreated cretin may have bands of increased density in the ends of the tubular bones such as one might expect to see in lead poisoning or osteopetrosis. All of these

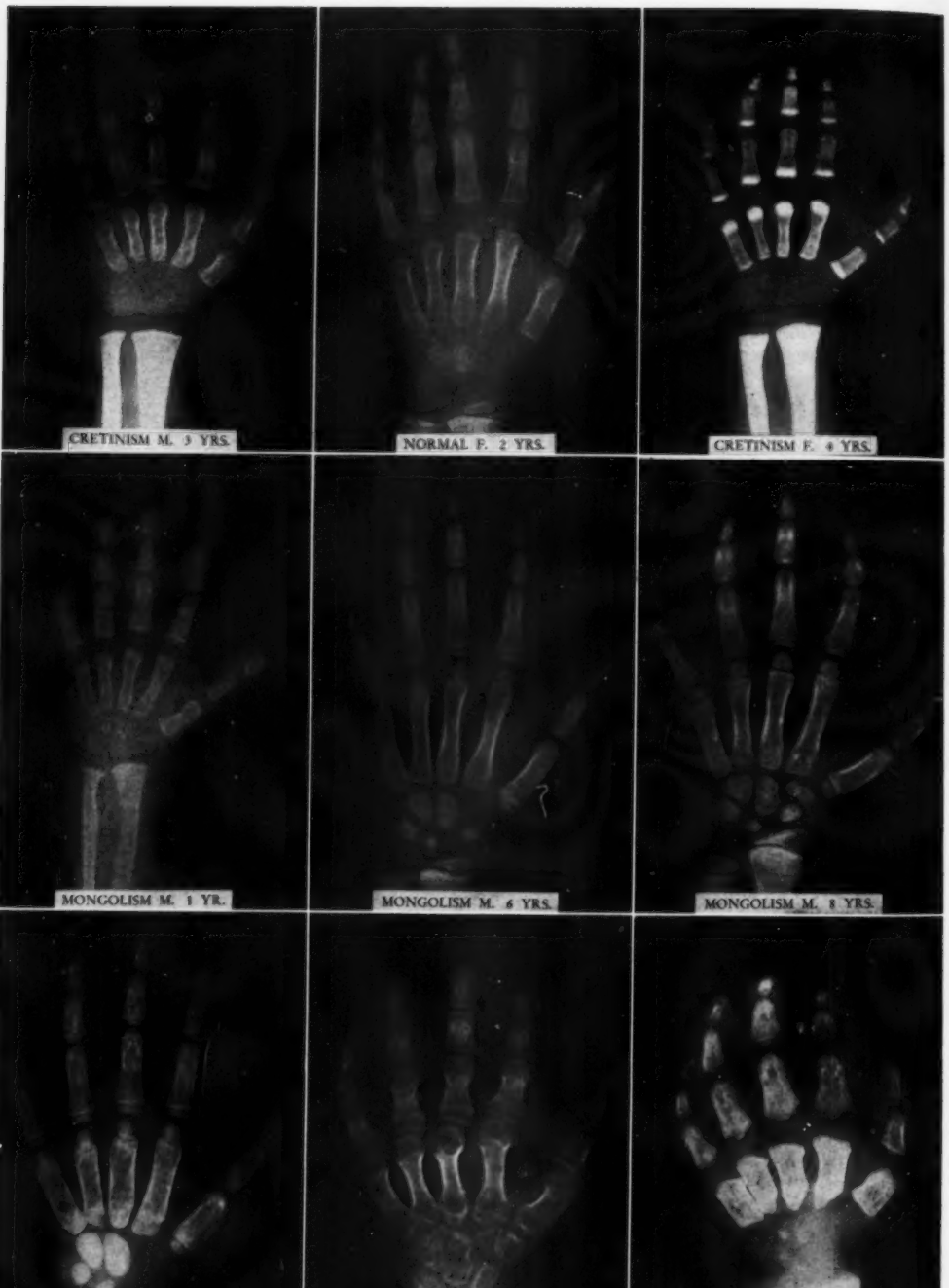
CRETINISM M. 3 YRS.
NORMAL F. 2 YRS.
CRETINISM F. 4 YRS.
MONGOLISM M. 1 YR.
MONGOLISM M. 6 YRS.
MONGOLISM M. 8 YRS.
ERYTHROBLASTIC ANEMIA M. 6 YRS.
ACHONDROPLASIA M. 13 YRS.
GARGOYLISM M. 3 YRS.

Figure 1.

changes, as well as their dramatic response to thyroid medication, are best studied in the bones of the hands and wrists.

The differential diagnosis between cretinism and mongolian idiocy may be facilitated by accurate interpretation of hand roentgenograms. In contrast to delayed ossification in the cretin is the relatively normal bone development seen in mongolism. Furthermore, the mongol may present fairly typical anomalies of the hands, chief among which is congenital shortening of the middle phalanx of a stubby, curved fifth finger. This abnormality, which represents valuable confirmatory evidence when present, was first described by Smith (2) in 1896, but references to it in roentgen periodicals are not numerous. Recent reviews of the subject by Hefke (3) and ourselves (4) have convinced us of the worth of this sign in the diagnosis of mongolism.

The "fibrocystic" bone lesions of hyperparathyroidism and polyostotic fibrous dysplasia, the peripheral degenerative changes of progeria, and the congenital anomalies, plus alterations in normal epiphyseal closure, associated with other endocrine dysfunctions constitute just a portion of the host of abnormalities in this category that are well shown in the bones of the hands. Hurxthal and Hare (5) have described changes in the metacarpals and phalanges which they maintain are practically pathognomonic of primary prepuberal hypogonadism.

CONGENITAL ANOMALIES

In addition to the anomalies of the hands which occur in conjunction with various endocrinopathies, certain other abnormalities in this category are worthy of note.

Dysostosis cleidocranialis is still regarded by some as a condition in which defective ossification takes place only in bones laid down in membrane. It is true that there is delayed ossification in the skull, manifested by multiple wormian bones, large fontanelles, and widely separated sutures. The clavicles are abnormal, varying from under-development to complete absence. But, as Brailsford (6) has emphasized, other bones are involved, and chief among these, as far as characteristic alterations in normal structure are concerned, are the hands. The ungual phalanges are short and cone-shaped, with failure of the usual prominent cancellous tufts to develop—the same tufts that are so exaggerated in acromegaly. The metacarpals, as well as the proximal and middle phalanges, have supernumerary epiphyses which fuse much earlier in life than the normal ones. All epiphyses appear broader than normal, so much so in the case of the terminal phalanx of the thumb that one gains the impression that this bone develops from two nuclei. The appearance of the hands in this unusual anomalous condition is quite striking and truly characteristic. It deserves more attention than it has been accorded in the past.

In the hands of the typical achondroplastic dwarf, the second to fifth metacarpals are short, stubby, and of nearly equal length. They are more parallel with one another than normal and, as in the case of the long bones, their ends may be quite bulbous. The phalanges likewise are extremely short and relatively broad.

The atypical forms of chondrodystrophic dwarfism show more characteristic changes, which may be of considerable significance. In Morquio's disease, for instance, the ends of the metacarpals and phalanges are grossly irregular, and the carpal bones, besides reflecting delayed skeletal development, have a striking crenated appearance. In Hurler's syndrome (gargoylism), the metacarpals in particular are unusually short and broad, the middle phalanges have an arrowhead configuration, and the trabecular pattern is very coarse and prominent.

Arachnodactyly is an interesting familial malady, apparently congenital in origin, which derives its name from the long, slender, spider-like fingers which characterize this entity. The roentgen appearance of the hands is unmistakable and when it is identified as such, attention immediately should be focused upon the patient's eyes and heart. Congenital dislocation of the lenses is almost invariably present, and as-

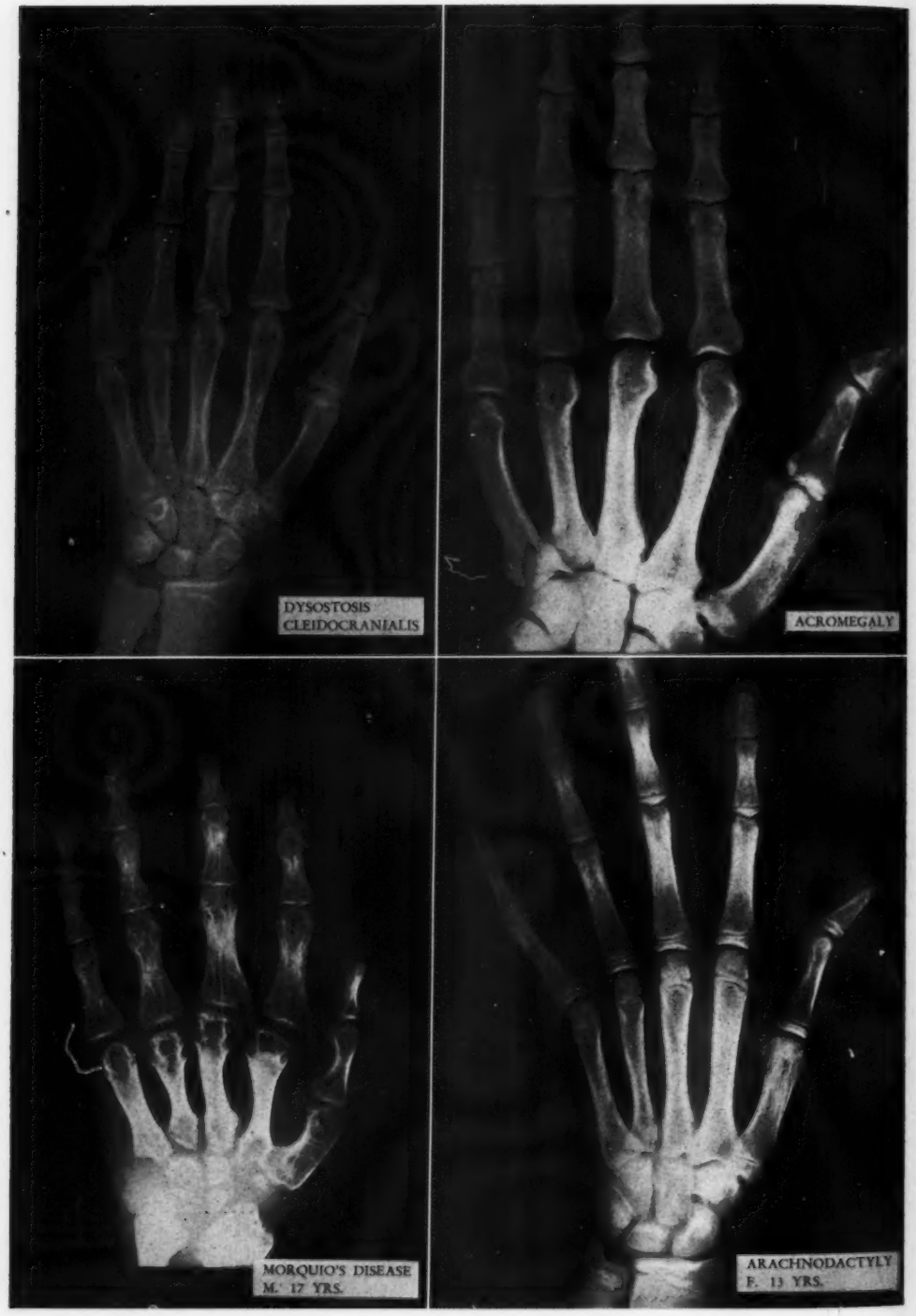
DYSOSTOSIS
CLEIDOCRANIALIS
ACROMEGALY
MORQUIO'S DISEASE
M. 17 YRS.
ARACHNODACTYLY
F. 13 YRS.

Figure 2.

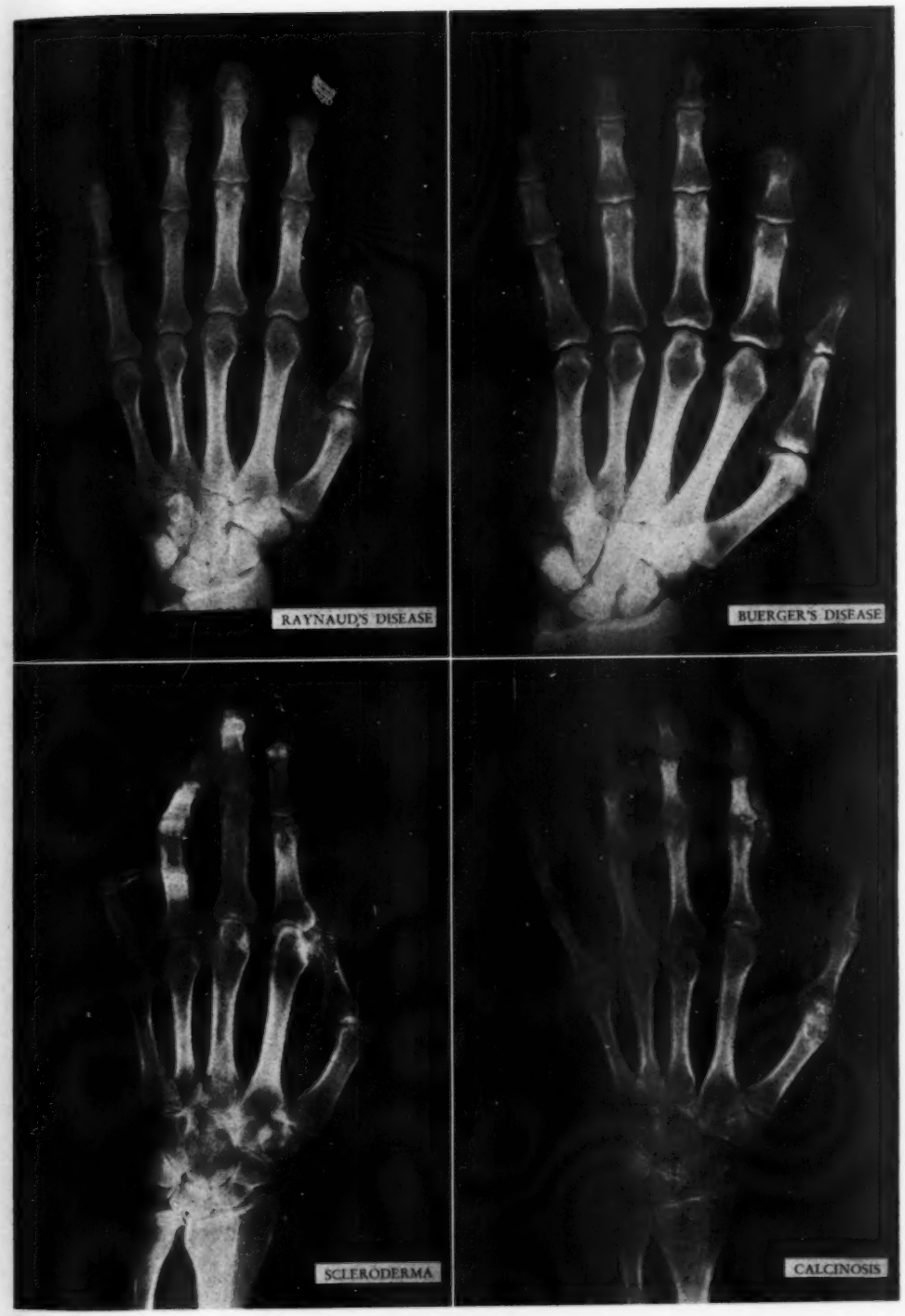
RAYNAUD'S DISEASE
BUERGER'S DISEASE
SCLERODERMA
CALCINOSIS

Figure 3

sociated congenital heart disease is very common. The great length of the metacarpals and phalanges may be still further accentuated by the presence of supernumerary epiphyses.

TROPHIC DISTURBANCES

Roentgenograms of the hands may reflect the presence of syringomyelia, leprosy, Raynaud's disease, erythromelalgia, thrombo-angiitis obliterans, arteriosclerosis, and diabetes, although it must be pointed out that the roentgen signs seen in these various diseases are quite similar and, therefore, of little differential diagnostic value. The outstanding feature common to all of the above conditions is slow, spontaneous amputation of portions of the phalanges or perhaps the entirety of one or more of these bones. Certain more selective diagnostic features have been described (7, 8, 9).

Scleroderma and acrosclerosis may also produce gradual, progressive absorption of the distal phalanges of the hands. In addition, there may be extensive osteoporosis of the juxta-articular portions of the metacarpals and phalanges, soft-tissue contracture deformities and, occasionally, soft-tissue deposition of calcium salts. The combination of these manifestations produces a fairly typical roentgen picture, which should not go unrecognized. The relationship of scleroderma and generalized calcinosis is of special interest, and the discovery of calcium in soft tissues of the hands should focus attention upon other regions of the body, especially when associated osseous changes are present.

CHRONIC GRANULOMAS

The bones of the hands may be involved by any form of non-specific inflammatory disease or the various specific granulomatous processes. Tuberculous dactylitis, commonly called spina ventosa because an involved metacarpal or phalanx appears to be distended by air, produces the most characteristic appearance. Identification of this lesion may lead to the discovery of tuberculosis elsewhere in the body.

In 1920 Jüngling (10) described an entity consisting of multiple cyst-like areas of destruction in the bones of the hands and feet with adjacent soft-tissue swelling and associated lesions of the skin and lymph nodes. He felt that this was another manifestation of tuberculosis and gave it the name of osteitis tuberculosa multiplex cystica. We now know that these bone changes and the bone lesions occasionally associated with Boeck's sarcoid are one and the same. The correlation of sarcoid lesions involving the bones, skin, lymph nodes, and lungs has been clearly demonstrated, but the etiological relationship to the tubercle bacillus is as obscure as ever.

Attention is called to the fact that the bone lesions in Boeck's sarcoid are not always punched-out and cystic in character. As Doub and Menagh (11) have pointed out, these lesions may begin merely as a coarsening of the trabecular pattern, following which areas of both cortical and central destruction appear. As the disease progresses, the destruction may assume extensive proportions.

Granulomatous lesions produced by pathogenic fungi may also involve the metacarpals and phalanges and, as in sarcoid, the findings of such lesions should prompt investigation of other regions of the body for additional manifestations of these diseases.

PULMONARY OSTEOARTHROPATHY

The existence of long standing chronic pulmonary or mediastinal disease may be suspected from a mere clinical inspection of the hands when clubbing of the terminal phalanges is observed. Roentgenograms may reveal the additional element of periosteal proliferation along the shafts of the metacarpals and phalanges—so-called hypertrophic pulmonary osteoarthropathy. The cause of this remote expression of pulmonary disease has not been satisfactorily explained, but its importance as a diagnostic sign cannot be minimized.

Pulmonary osteoarthropathy occurs with greater frequency in non-tuberculous lesions of the chest; in fact, we have been un-

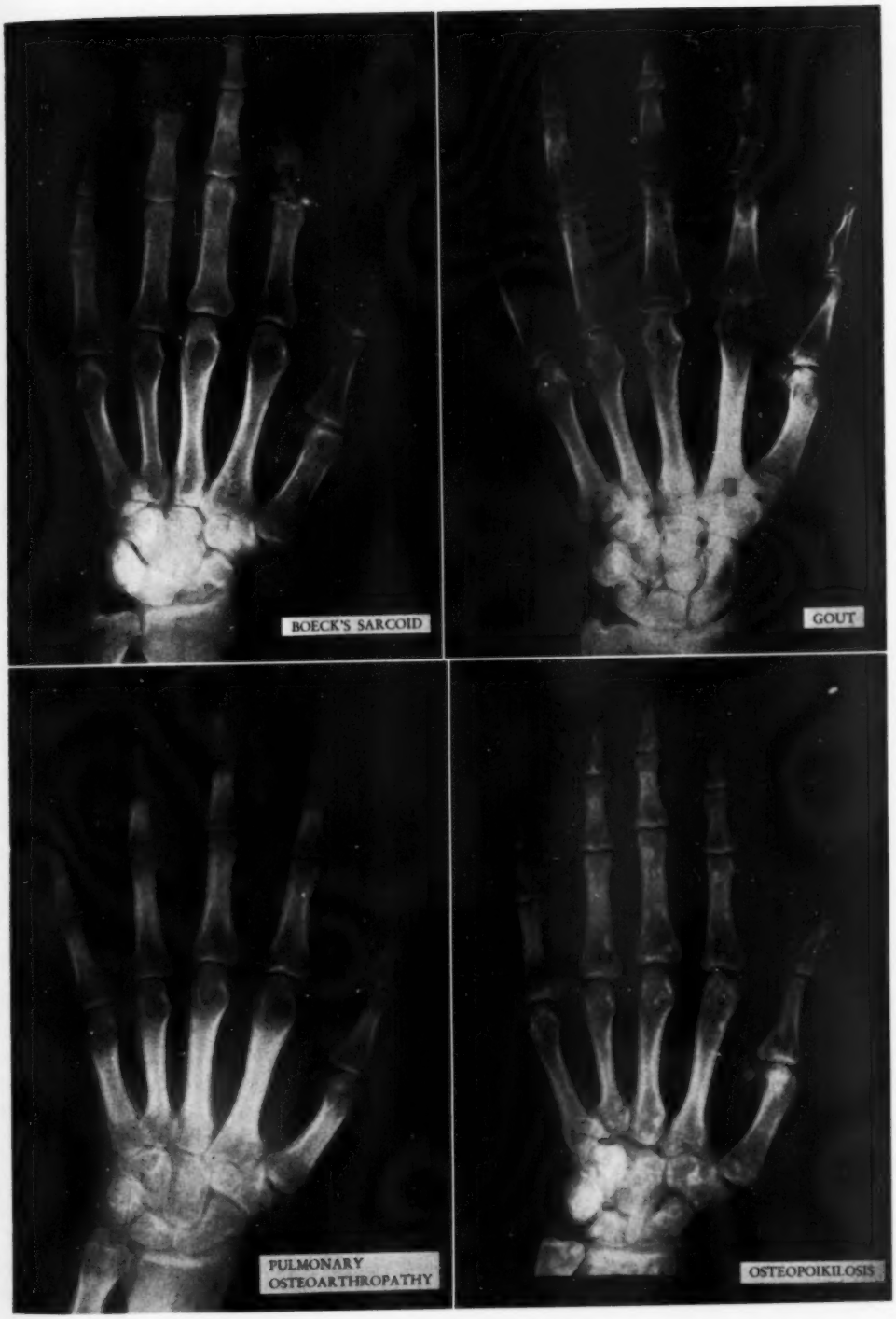
BOECK'S SARCOID
GOUT
PULMONARY
OSTEOARTHROPATHY
OSTEOPOIKILOSIS

Figure 4.

able to find a single instance of its occurrence in uncomplicated pulmonary tuberculosis in the case records of University Hospital.

Probably the most remarkable feature about pulmonary osteoarthropathy is the fact that its severity, regression, and progress vary directly with the degree of pulmonary involvement. Roentgenograms of the hands may thus serve as fairly accurate indicators of the success or failure of any therapeutic procedure directed toward the causative pathological process within the thorax. Patients in whom the pulmonary lesion is entirely eradicated will show complete disappearance of the bone changes. When, as is much more often the case, the pulmonary lesion becomes progressively worse, the periosteal proliferation becomes accentuated and quite dense. In severe cases this dense new bone formation is difficult to distinguish from the underlying cortical bone. To avoid diagnostic and, more particularly, prognostic error, the roentgenologist must be extremely careful to make this distinction.

HEMOPOIETIC AND BLOOD DISEASES

Among the diseases of the blood and blood-forming tissues, hemophilia, leukemia, and the chronic hemolytic anemias may produce valuable roentgenographic signs in the osseous system. The moth-eaten destructive lesions of leukemia occasionally are found in the bones of the hands but are much more clearly recognized in the long bones. Hemophilia expresses itself in the form of articular irregularities in the larger joints. On the other hand, erythroblastic anemia tends to involve the entire skeletal system in such a manner that its roentgenographic picture is unmistakable. In no portion of the skeleton is this picture more clearly demonstrated than in the hand. The metacarpals and phalanges take on a characteristic rectangular shape, the medullary canals are dilated, and the cortices are thinned. The shafts of the bones are traversed by a coarse, irregular meshwork of dense, broadened trabeculae which stands out in bold relief against an over-all background of atrophic bone substance. Whereas this pattern is seen in the ends of the long bones, it is very prominent throughout the entire length of the metacarpals and phalanges and thus produces a striking effect that can be recognized at an earlier stage in the disease process. Moreover, the delayed ossification that invariably accompanies the malady can best be appreciated in the carpal bones.

Only isolated instances of similar bone changes have been reported in sickle-cell anemia and chronic hemolytic jaundice. We have not encountered them in such cases as have come to our attention.

MISCELLANEOUS LESIONS

The value of roentgenography of the hands in the diagnosis and prognosis of the various types of chronic non-specific arthritis cannot be overestimated. Roentgen signs of rheumatoid arthritis, consisting of osteoporosis, reduction of cartilage spaces, and areas of subchondral bone destruction, usually make themselves apparent in the proximal interphalangeal joints before they appear in other joints. When these changes are seen in and adjacent to the distal interphalangeal joints alone, the possibility of so-called arthropathia psoriatica may be reasonably considered. This implication is justifiable because uncomplicated rheumatoid arthritis seldom, if ever, involves the distal interphalangeal joints to the exclusion of all others. Osteo-arthritis usually manifests itself first in the distal interphalangeal joints, and the ridges of osteophytes that appear give rise to the classical, clinically recognizable swellings known as Heberden's nodes.

Gout reflects a disturbance in purine metabolism and, although tangible roentgenographic evidence of this disease is commonly associated with the feet, the bones of the hands may show intramedullary and extramedullary destructive changes due to adjacent tophi which may be just as extensive as those in the lower extremities.

Chondromata and solitary cysts are not

uncommonly encountered in the bones of the hand. Curiously enough, the occurrence of chondromata in the hands is occasionally associated with the presence of similar lesions in other bones. Other neoplastic lesions appear so rarely in the hand bones that they will not be considered.

Osteopoikilosis, osteopetrosis, and melorheostosis are some of the additional abnormalities that are occasionally encountered in the hands and wrists. The roentgen appearance of each of these entities is characteristic enough to permit accurate diagnosis from hand roentgenograms alone. Tuberous sclerosis sometimes produces rarefactions in the phalanges.

SUMMARY

An attempt has been made to focus well deserved attention upon roentgenograms of the hand as a source of important diagnostic information. In addition to purely local pathological processes, the alterations of normal carpal, metacarpal, and phalangeal structure which reflect the presence of remote systemic disease entities are worthy of careful consideration. A single dorsal-palmar projection of the hand is generally more valuable in this respect than other portions of the skeleton because of the technical simplicity of the procedure, the absence of confusing overlapping shadows, and the relative rapidity of change in the hand and wrist bones during the period of maturation.

Although many of the abnormalities discussed are rarely encountered, the hand changes in certain instances are virtually diagnostic, and familiarity with them will bring about prompt evaluation and accurate classification of the disease process responsible for their production.

Dr. M. Cooperstock, Marquette, Mich., and Capt. A. H. Joistad, M.C., A.U.S., supplied the illustrative roentgenograms of arachnodactyly and osteopoikilosis respectively.

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Tuberculosis of the Greater Trochanter and Its Bursa[1]

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TUBERCULOSIS of the greater trochanteric bursa is a rare condition and is usually secondary to tuberculous osteomyelitis of the greater trochanter. A perusal of the literature substantiates these observations.

The early writings on trochanteric bursitis are, for the most part, case reports of inflammatory lesions, without mention of the etiologic agent. It was not until 1904 that the concomitant involvement of the greater trochanter was recognized by Wieting (1), who believed, as did several later writers, that the primary infection is in the trochanter, whence it spreads to the bursa. Clopton (2), Keith (3), and others supported this view and pointed out that, since the greater trochanter develops as an epiphysis, it is as such susceptible to tuberculous infection, which would further establish the probability of primary involvement of the bone and secondary invasion of the bursa. Cone (4) in 1911 and Swindt (5) in 1921 stressed the significance of trauma as an etiologic factor and noted the rarity of tuberculosis of the greater trochanter in children. In 1933 Meyerding and Mroz (6) reported a series of 19 cases of tuberculosis of the greater trochanter and its bursa. Fourteen of these were on the right side, which, they believe, favors trauma as playing an etiologic role. In 73 per cent of the series evidence of tuberculosis was found elsewhere in the body. Donovan and Sosman (7) in 1942 reported 5 cases, in all of which there was evidence of tuberculosis elsewhere, healed, active, or inactive. This is true, also, of the cases to be recorded here. Two of the cases reported by Meyerding and Mroz and one of Sosman and Donovan involved only the bursa. All writers agree that complete extirpation of all infected tissue, with immobilization of the affected part, followed by body-building postoperative care, is the treatment of choice.

[1] From the Department of Roentgenology, Henry Ford Hospital, Detroit, Mich. Accepted for publication in March 1944.

CLINICAL FINDINGS

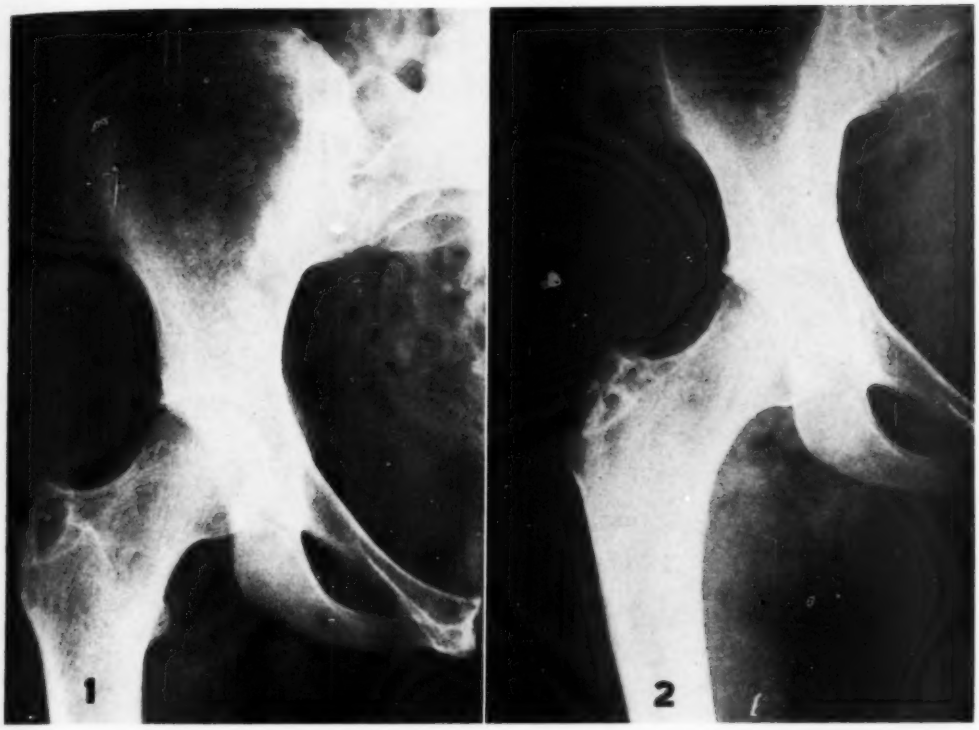
Tuberculosis of the greater trochanter and the greater trochanteric bursa may occur at any age and in either sex but, as previously noted, is unusual in children. Occupation has no bearing on the incidence. The usual complaint is mild pain in the involved leg over a long period of time, with intervals of quiescence. Often there is a draining sinus over the trochanteric area. Some patients give a history of trauma before the onset of symptoms, but frequently this is difficult to evaluate.

Examination shows slight swelling over the trochanteric area, with tenderness to pressure, but no heat or redness. Weight-bearing is usually painless, and motion of the hip is free. Evidence of tuberculosis, active or inactive, can be demonstrated elsewhere in the body in most of the cases.

There is a strong tendency for the condition to recur and, if a series of cases is followed over a period of years, a high percentage of recurrences will be found. Some of these will show extension of the process, with involvement of the neck and head of the femur. The joint itself may finally be involved. Where the disease is limited to the bursa, the percentage of cures is believed to be somewhat higher.

ROENTGEN FINDINGS

The first roentgen evidence of tuberculosis of the greater trochanter may be a small fleck of calcium in the bursa or a minimal area of destruction in the outermost part of the trochanter. These are often difficult to demonstrate with the usual bone technic, and may easily be missed. Donovan and Sosman (7) recommend a light technic comparable to the soft-tissue technic used to demonstrate calcification



Figs. 1 and 2. Case 1: Destruction of the greater trochanter of the right femur with calcification of the bursa. Figure 2, ten months after operation, shows evidence of repair in the previously involved area. No evidence of activity is present.

around the shoulder. In this manner small calcium deposits in the bursa and early erosion of the cortex can be demonstrated.

The usual appearance on the roentgenogram is an area of destruction in the greater trochanter with osteoporosis of the adjacent bone. There is usually some soft-tissue swelling of the area, with calcium deposits in the bursa. Sometimes an involucrum is formed in the soft tissues lateral to the trochanter. This, however, is found in long-standing cases in which an operation has been done, or in those cases in which there has been a draining sinus for a long period of time, and is probably the result of secondary infection or injury to the periosteum.

DIFFERENTIAL DIAGNOSIS

Simple inflammatory (non-specific) bursitis of the trochanteric bursa can and does occur and must be differentiated from tuberculous involvement. The symptoms are more acute and are usually promptly relieved by simple treatment. The presence of acute symptoms, absence of a sinus tract, and/or absence of involvement of the trochanter, along with prompt response to simple remedial measures, aid in the differential diagnosis.

Differentiation from tumors involving the trochanter does not usually offer much difficulty. In one of our cases (Case 1), however, a diagnosis of neoplasm of the femur was made at another hospital and the patient was given deep therapy. Later a biopsy proved the condition to be inflammatory.

Non-specific osteomyelitis involving the greater trochanter offers a problem in differential diagnosis, and in certain stages the roentgen picture is identical with that seen in tuberculosis. In such cases the clinical course and past history are helpful.

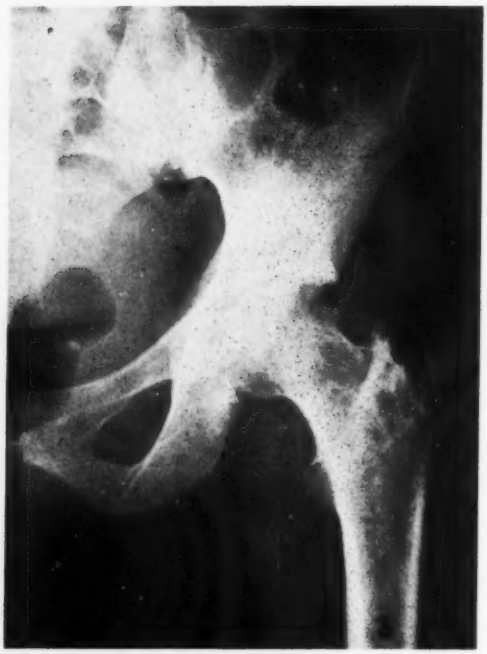


Fig. 3. Case 2: Almost complete destruction of the greater trochanter with sequestration; irregularity and narrowing of the joint space.

CASE REPORTS

CASE 1: Mrs. J. C., a 33-year-old housewife, was admitted to the Henry Ford Hospital in February 1943, with a draining sinus in the region of the right greater trochanter. In June of 1941 she had bruised her right hip. A painless swelling developed shortly thereafter in this region, and its persistence brought her to a physician. A diagnosis of neoplasm of the right femur was made, and several deep x-ray treatments were given to the right hip before a biopsy showed the condition to be inflammatory. The patient was subsequently operated on at another hospital and placed in a cast for five months, after which she remained well until November 1942. The swelling then reappeared, and in January 1943 a sinus developed in the operative scar.

On examination the patient appeared to be in excellent physical condition. She walked without any apparent limp and without pain. There was no limitation of motion of the hip joint. In the region of the right greater trochanter was a draining sinus, with slight soft-tissue swelling and tenderness. A roentgenogram (Fig. 1) taken at this time showed a destructive process involving the greater trochanter, slight osteoporosis of the surrounding bone, and calcification in the region of the bursa. There was thought to be a possible sequestration of the tip of the trochanter. The chest film showed calcified tuberculosis.

Operation was performed on March 10, 1943, when the sinus tract and all infected tissue were excised as thoroughly as possible. The microscopic diagnosis was tuberculosis.

When last seen, in January 1944, the patient was entirely well. Roentgenograms taken at that time showed regeneration in the previously involved areas (Fig. 2).

CASE 2: A. S., a 43-year-old housewife, came to the hospital in January 1944, complaining of pain in the left hip. She had first noticed some discomfort in this region twenty years before admission. This bothered her occasionally, but during the past ten years it had become troublesome and a slight limp had developed. She had spent a month in bed twenty years ago, with pulmonary tuberculosis.

Examination showed slight restriction in motion of the left hip, accompanied by pain, in all directions. There was definite tenderness on pressure over the greater trochanter with some fullness anteriorly. There was also slight atrophy of the thigh.

Roentgenograms (Fig. 3) showed a destructive process involving the greater trochanter of the left femur, with calcification laterally and sequestration. There were also osteoporosis of the surrounding bone and narrowing and irregularity of the joint space. The chest film showed calcified tuberculosis in both apices.

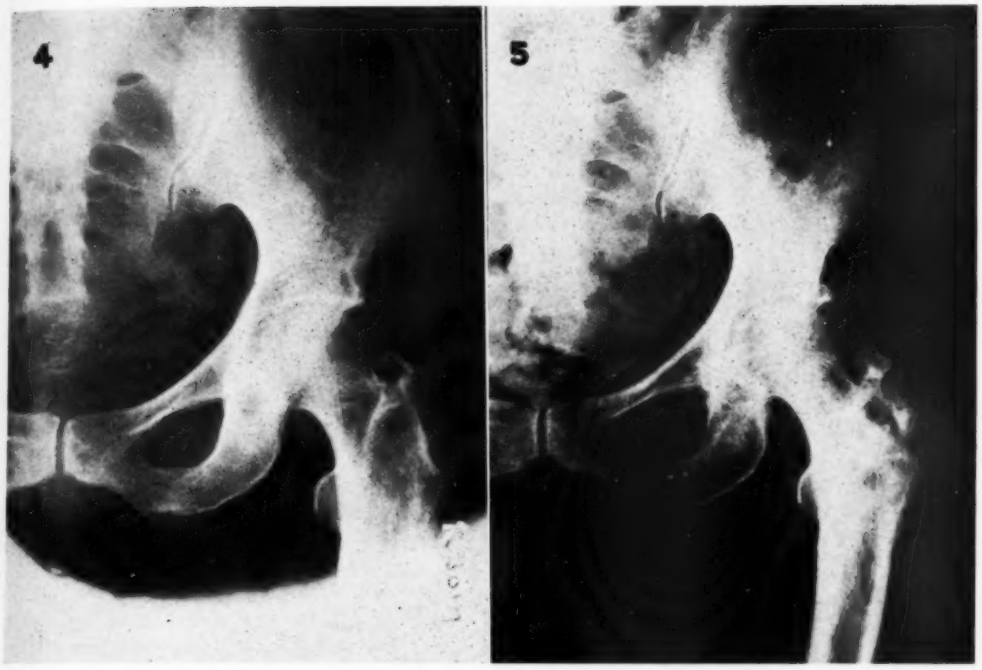
The left leg and hip were immobilized and the patient put on complete bed rest. Operation has not yet been done because of the involvement of the joint. If this does not subside, a fusion of the hip may be necessary, along with complete removal of all infected tissue.

CASE 3: L. S., a 40-year-old housewife, was first seen in August 1933. Prior to admission she had undergone two operations on the left hip for drainage of abscesses, one ten and the other four years previously. Three months before admission she noticed some swelling in the trochanteric area. There had been very little pain, and this occurred at night after retiring.

Examination showed slight swelling anterior to the greater trochanter. The swelling itself was not tender, but there was tenderness over the greater trochanter. There was no limitation of motion of the hip and no pain on movement. A roentgenogram (Fig. 4) taken at this time showed a destructive process involving the greater trochanter and the cortex just below. The chest film showed calcified tuberculosis.

At operation wide excision was done and the bone was curetted. The pathologist reported a diagnosis of tuberculosis.

Following this the patient was well for a time, but the condition recurred successively in June 1934, September 1935, and again in September 1939. In June 1939 urinary symptoms had appeared and urine culture had been positive for tuberculosis. A right nephrectomy was done at that time. In September 1939 the patient began to have pain on



Figs. 4 and 5. Case 3. Figure 4 shows several areas of destruction in the left femur, in the greater trochanter, and in the cortex just below. Figure 5, five years later, shows involvement of the femoral head and neck with narrowing of the joint space.

movement of the left hip, with limitation of motion in all directions. Roentgenograms (Fig. 5) showed involvement of the head of the femur and narrowing of the joint space.

A fusion operation (arthrodesis and sliding bone graft) was done and the patient was symptom-free until late in 1941, when she was seen at another hospital complaining of pain in the left knee. There was no recurrence in the trochanter or hip at that time.

CASE 4: L. B., a 27-year-old housewife, was first seen in 1925, with enlarged cervical and inguinal nodes and a draining sinus over the right greater trochanter. These had been present for several years. The hip joint was freely movable; there was no pain on movement and only slight tenderness on pressure over the greater trochanteric bursa.

Roentgenograms (which have unfortunately been lost) showed calcification in the trochanteric bursa and a small area of destruction in the outermost portion of the trochanter. The chest film showed calcified tuberculosis.

At operation the sinus tract and all infected tissue were removed and the trochanter was curetted. The cervical and inguinal nodes were also incised and curetted. The pathological report described typical tuberculous tissue.

In 1928 a sinus tract again appeared in the region of the trochanter and was excised. The patient had no further trouble until 1938, when a cold abscess developed in the right buttock. This was incised and drained, and the patient was not seen again.

Roentgenograms (Fig. 6) taken in 1938 showed some thickening of the bone along the greater trochanter laterally, suggesting bone production in this area. Some calcification in the soft tissues inferior to the right ischium and some irregularity of the inferior margin of the ischium were also demonstrable. These findings were believed to be due to old infection in these areas. There was no evidence of recent involvement.

SUMMARY AND CONCLUSIONS

1. Tuberculosis of the greater trochanteric bursa is a rare condition and is usually secondary to tuberculosis of the greater trochanter.

2. The symptoms are usually mild, and often intermittent in nature. Weight-bearing is usually painless and motion of the hip free.

3. Evidence of tuberculosis can be demonstrated elsewhere in the body in most of the cases.

Fig. 6. Case 4: Right hip ten years after operation for tuberculosis. There is slight thickening of the bone of the greater trochanter. No evidence of any recent involvement.

4. Roentgenograms show a small area of destruction of the outer margin of the greater trochanter with a surrounding area of osteoporosis. There may also be small calcium deposits in the greater trochanteric bursa, and soft-tissue swelling may be seen over this area. If the infection progresses, the roentgenograms may show involvement of the femoral head and neck, and finally of the hip joint.

5. The accepted treatment is complete extirpation of all infected tissue, with immobilization of the affected part. This is followed by body-building postoperative care.

6. The condition has a tendency to recur even after seemingly adequate treatment, with formation of a chronic draining sinus and secondary infection. Those cases in which the bursa alone is involved seem to have the best prognosis.

7. Four cases of tuberculosis of the greater trochanter and its bursa are presented to illustrate these conclusions.

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Thoracic Manifestations of Sarcoidosis[1]

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THE CUTANEOUS lesions long known as *lupus pernio* and the glandular, ocular, osseous, mucous membrane, and systemic disease known as *sarcoid* were first described as one clinicopathological entity by Schaumann (9, 10) in 1914. He demonstrated clearly the lung alterations occurring in sarcoidosis which could be shown radiographically and rejected the concept that the changes were due to residues of pneumonia or to a dissemination of tuberculous nodules. He directed attention to the close similarity between the roentgen appearance in so-called chronic miliary tuberculosis and certain cases of sarcoidosis, although, in the latter, strand-like infiltrations radiating from the hilar regions were more characteristic.

It is now well recognized that the histologic unit of sarcoidosis is the so-called "hard tubercle," which consists of a collection of pale-staining epithelioid cells, with frequent giant cells, in which there is no peripheral inflammatory zone. There is no necrosis. Calcification, when it occurs, is very fine and is not conglomerate. The predilection of sarcoid tissue for the lymphatic structures in the interlobular septa explains the diffuse streaking seen in the pulmonary roentgenograms. As repeatedly demonstrated, sarcoid tissue ultimately replaces lymphoid structures. Kuznitzky and Bittorf (5) in 1915 and many subsequent authors (3, 6, 7) have further clarified the roentgenologic appearance of sarcoidosis and have shown the remarkable disproportion between massive infiltrations and minimal—frequently absent—physical signs and symptoms. Although cough and expectoration occur occasionally, febrile reactions, as a rule, are slight. Râles are rarely heard, and only in extreme enlargement of the superior mediastinal and peribronchial lymph nodes can any dullness or modification of the breath sounds be obtained. There is a distinct tendency, in some cases, for the radiographic shadows to diminish and even disappear completely; in others, however, the shadows may persist without perceptible alterations for many years. It is not unlikely that a large number of instances of "chronic, or healed, miliary tuberculosis" belong to this group.

There have been reports of cases of right heart failure induced by diffuse pulmonary sarcoidosis (1, 8). Furthermore, the heart is not infrequently involved, and invasion of the myocardium or pericardium by sarcoid has been found in a total of 28 recorded autopsies. Recognition of these lesions during life is often impossible, due to the scattered distribution of the infiltrations. There are, however, numerous instances of cardiac enlargement which, in the absence of murmurs or hypertension, may represent myocardial sarcoidosis. Conduction defects, arrhythmias, and variable degrees of myocardial failure have been described. In two of the cases in the present group distinct cardiac enlargement appeared while the patients were under observation for systemic sarcoidosis.

Pulmonary lesions in sarcoidosis occur with great frequency. They were found in 29 of 31 cases carefully studied by Longcope (7), and this proportion has been maintained in other published series.

In a follow-up of 37 cases studied over a space of several years, King (4) found that the radiographic pulmonary lesions cleared completely, or almost completely, in 60 per cent of the cases in from seven weeks to three years, with an average of twenty-two months. Following the disappearance of pulmonary lesions, recurrences in the lung have been rare. The appearance of new lesions in the lungs, however, as hilar

[1] From the Medical Services and the Department of Radiology, The Mount Sinai Hospital, New York. Presented before the New York Roentgen Society in January 1944. Accepted for publication in March 1944.

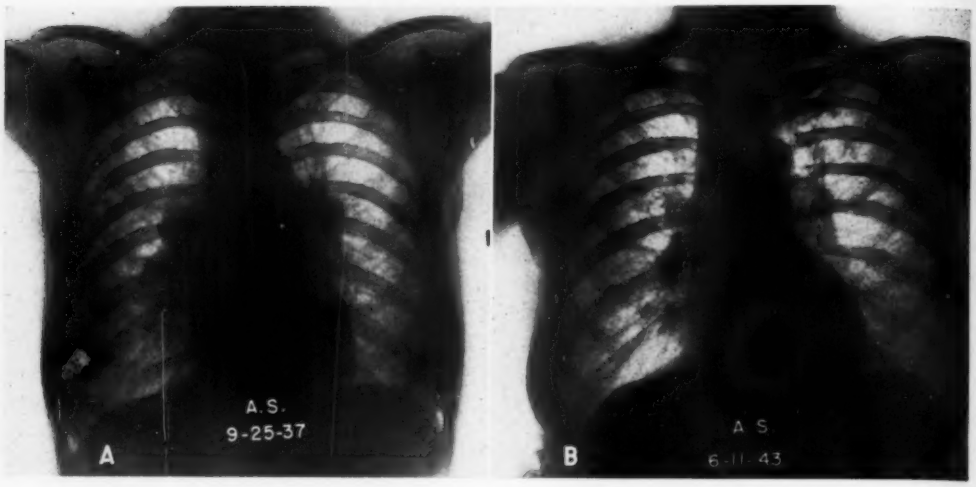

Fig. 1. Case 2. This patient had a uveoparotid syndrome (Heerfordt). Large hilar and paratracheal nodes were demonstrated in 1937. The nodes slowly receded until in 1943 there was only slight residual lymphadenopathy.

adenopathy is receding, is common. Fibrosis demonstrated roentgenologically in the mediastinal lymph nodes and lungs is not common. On the other hand, Klemperer (quoted by Bernstein and Oppenheimer, 1) pointed out that hyalinization and fibrosis are found at necropsy.

The series upon which the present paper is based consists of 12 cases. Due to the close resemblance of the roentgen appearance in this disease to other conditions, chiefly tuberculosis, and the absence of conclusive radiologic features, we have not included for description any cases that were not confirmed by histologic evidence. The course of the thoracic manifestations as observed roentgenologically is not pathognomonic. Tendency to spontaneous healing cannot be deemed a diagnostic feature, inasmuch as it is observed in miliary tuberculosis, erythema nodosum, rheumatic pneumonitis, and eosinophilic infiltrations in the lungs, all of which may present a roentgen picture indistinguishable from that of sarcoid. On the other hand, pulmonary infiltrations which persist without change are not necessarily characteristic, since they may occur in diffuse but stable tuberculosis.

Since the pathologic process tends to change constantly and organ involvement is largely fortuitous, the roentgen features are grouped only for convenience in description and not to suggest that there are corresponding static phases of the disease.

The *first group* includes cases with bilateral, frequently symmetrical, enlargement of the hilar and bronchial lymph nodes without evident pulmonary infiltration.

CASE 2: A. S., a 34-year-old woman, presented a uveoparotid syndrome (Heerfordt, 2) and generalized lymphadenopathy. Biopsies of lymph nodes, iris, and tonsils all revealed sarcoidosis. Roentgen examination of the chest in September 1937 showed huge nodes in both hilar and paratracheal areas (Fig. 1A). By November 1937 the nodes were definitely smaller and continued receding during the next year. By June 1943 there was slight residual enlargement of the nodes; pulmonary markings were slightly exaggerated, particularly in the right upper lobe, but there was no definite infiltration (Fig. 1B).

A *second group*, probably the largest, includes those cases with mediastinal adenopathy and variable degrees of infiltration into the pulmonary parenchyma. The infiltration ordinarily is strand-like and extends out more or less symmetrically from the hila. In other instances dense streaks are less apparent, but the infiltration is

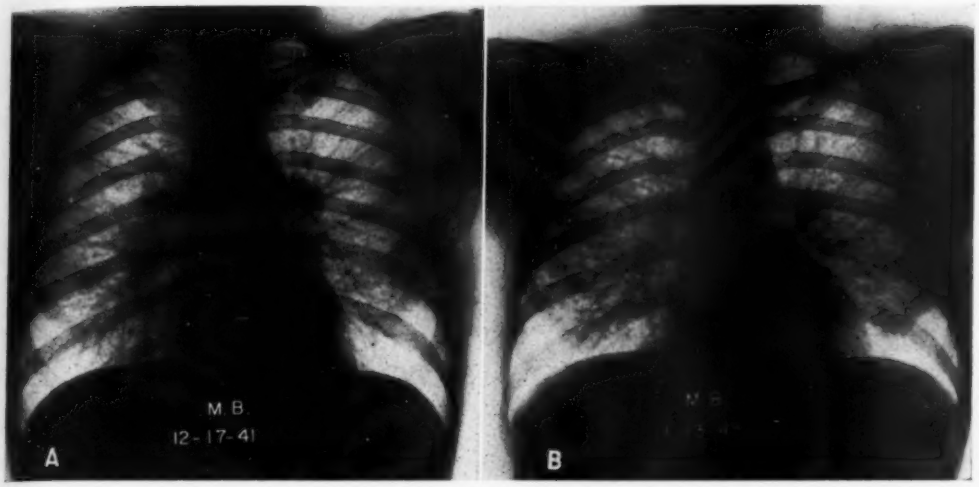

Fig. 2. Case 4. The patient was an asymptomatic male with proved sarcoidosis. In December 1941, hilar nodes were moderately enlarged. In the course of one year, the nodes receded but pulmonary infiltration became more extensive, having a reticulated appearance.

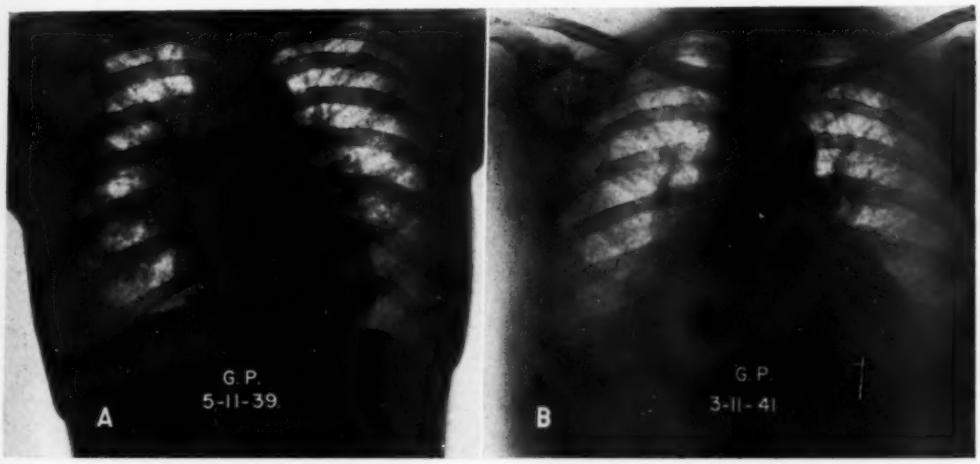

Fig. 3. Case 6. Generalized sarcoidosis with hilar adenopathy since 1936 in a colored female. By 1939, the nodes were smaller, but pulmonary infiltration was more extensive. In 1941, pulmonary infiltrations are seen to have disappeared but the right hilar and paratracheal nodes were greatly enlarged. In addition, there was a marked increase in the size of the cardiac shadow.

interlaced, resulting in a reticulated appearance. Either variety may progress into or be associated with confluent patchy infiltrations in the lungs.

CASE 4: M. B., a man of 27, was completely asymptomatic but Army induction resulted in the discovery of enlargement of the lymph nodes at the root of each lung. There was generalized adenopathy, and biopsy of a supraclavicular lymph node showed sarcoidosis. The skin reaction to tuberculin was negative. Chest roentgenograms in December 1941 revealed large hilar nodes and slight pulmonary infiltration, especially in the lower lobes (Fig. 2A). The nodes slowly decreased in size but the pulmonary disease became more extensive. In January 1943 (Fig. 2B) the nodes were nearly normal in size but extensive reticulated pulmonary densities were present. The patient was examined last in August 1943, when the nodes were normal in size and there was perhaps slight recession in the pulmonary infiltrations.

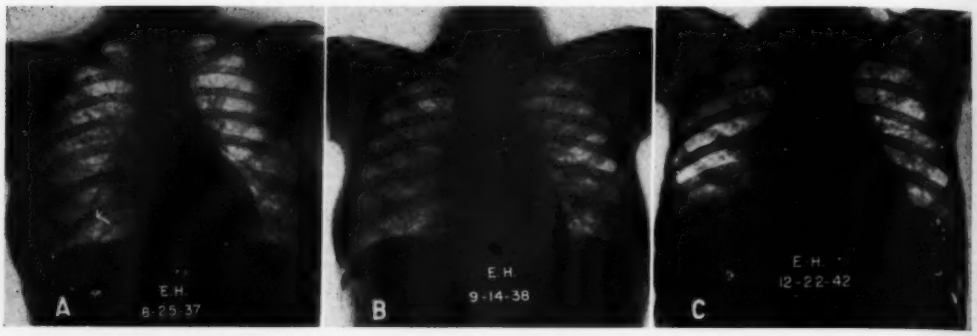

Fig. 4. Case 7. Diffuse sarcoidosis in a female, showing faint reticulated densities in the lungs in 1937, a miliary infiltration in 1938, and more confluent densities distributed irregularly in 1942. There was increase in the size of the cardiac shadow.

CASE 6: G. P., a 45-year-old Negress, had generalized sarcoidosis including extensive lesions of the skin, lymph nodes, and bones. The skin reaction to tuberculin was negative. A positive blood Wassermann reaction was present despite intensive antisyphilitic treatment in previous years. A chest roentgenogram in April 1936 revealed enlarged hilar and paratracheal nodes. In May 1939 the nodes were less distinct and somewhat smaller, but there were diffuse strand-like infiltrations extending out from both hila (Fig. 3A). By June 1940 the pulmonary infiltrations had disappeared, but the hilar nodes were again larger. The cardiac shadow was increased. In March 1941 (Fig. 3B) the right hilar nodes were very large. Enlargement of the heart was still present.

Case 6 illustrates a recession followed by a considerable increase in the size of the hilar nodes. While the nodes became smaller, pulmonary infiltrations appeared, disappearing again as the nodes enlarged.

A *third form* of roentgen finding is represented by miliary lesions, easily simulating and often roentgenologically indistinguishable from chronic miliary tuberculosis. Mediastinal adenopathy may be present or absent, or may disappear under observation.

CASE 7: E. H., a white female of 28 years, was found to suffer from diffuse sarcoidosis and diabetic glomerulonephritis (Kimmelstiel). Inguinal node biopsy confirmed the diagnosis of sarcoidosis. The skin reaction to tuberculin was positive. X-ray examination of the chest in August 1937 revealed slight enlargement of the hilar nodes and diffuse reticulated densities in both lungs (Fig. 4A). In September 1938 the pulmonary infiltrations were miliary in type, while the nodes were unchanged in size (Fig. 4B). By December 1942 (Fig. 4C) the miliary appearance was less distinct. There were indefinite confluent homogeneous shadows in the right upper, right lower, and left lower lobes. There was a small pleural effusion on the right side. The cardiac shadow was now enlarged. A calcified node was seen in the right hilum for the first time. The patient was examined again in March 1943, but no significant change was found.

The salient features in this case are the varying quality of infiltration, the presence of pleuritis, cardiac enlargement, and the probable association with tuberculosis as indicated by calcification of a hilar node.

A *fourth type* of the disease shows a discrete nodular infiltration with or without hilar adenopathy.

CASE 8: L. R. was a 17-year-old Puerto Rican male, complaining of moderate cough and weight loss with slight fever. There was no palpable adenopathy at the initial examination but at a later date biopsy of a supraclavicular node disclosed sarcoidosis. The skin reaction to tuberculin was negative. Roentgen examination of the chest in January 1943 revealed large hilar nodes, especially on the right side, with very slight if any infiltration of the lungs (Fig. 5A). In June 1943 the nodes were unchanged but the lung infiltrations were more extensive. By September 1943, the nodes had begun to recede but the pulmonary infiltrations had become larger. In January 1944 (Fig. 5B) the nodes were distinctly smaller, while the pulmonary infiltrations were extensive, consisting of nodules of varying size with irregular confluence.

CASE 9: J. J., a 36-year-old Negro, had diffuse skin lesions which on biopsy proved to be sarcoidosis. He complained of fever, anorexia, cough, and weight loss for three months. The Mantoux test was positive. The patient exhibited no elevation in temperature while under observation in the hospital. Sputum examinations revealed no tubercle

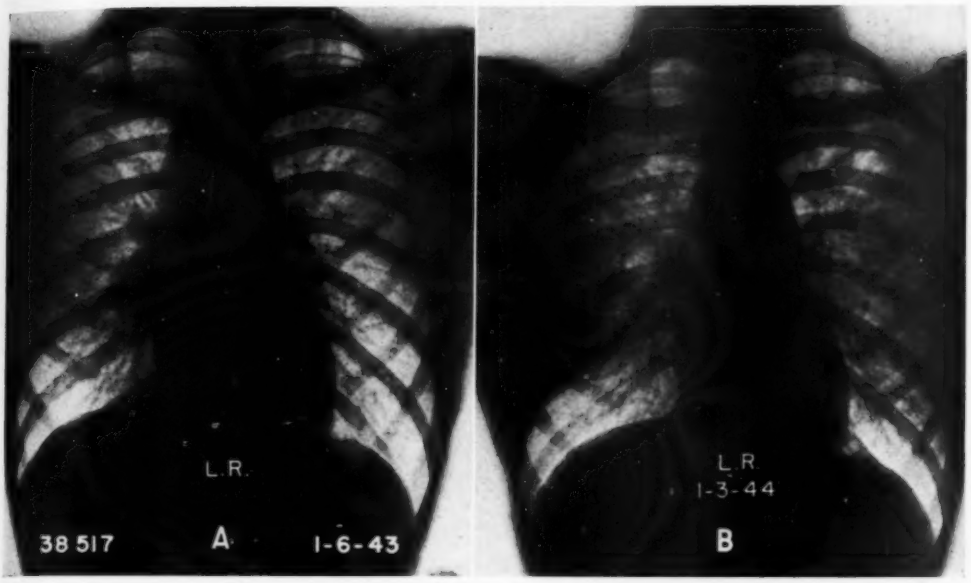

Fig. 5. Case 8. The patient was a male 17 years old with hilar and paratracheal adenopathy in January 1943. One year later, the nodes had diminished in size but extensive patchy nodular infiltrations had appeared.

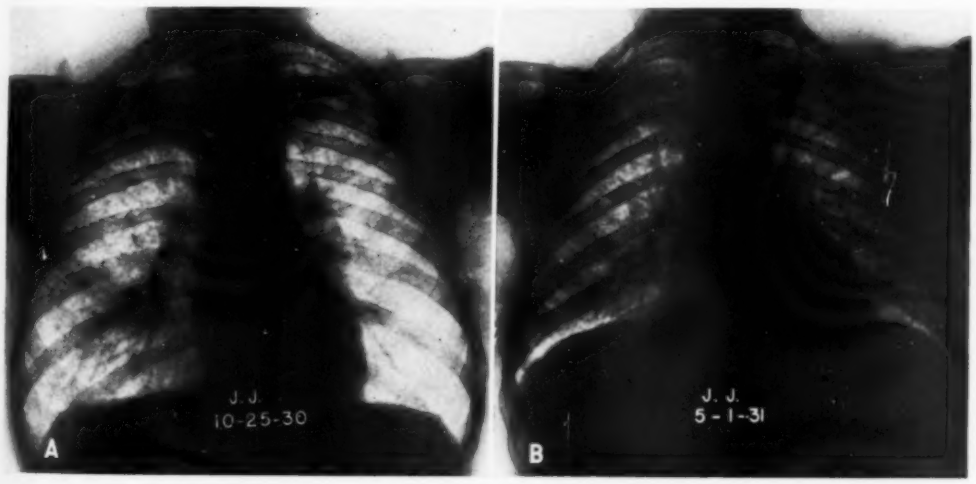

Fig. 6. Case 9. Skin sarcoidosis in a male was associated with submiliary infiltrations in the lungs. These were reversible and had cleared to a considerable degree six months later.

bacilli. X-ray examination of the chest in October 1930 showed diffuse submiliary infiltrations throughout both lungs, particularly in the right upper lobe (Fig. 6A). By May 1931 the lungs had cleared considerably (Fig. 6B).

A *fifth type* of roentgen appearance is that of diffuse and confluent infiltrations which may represent a transition from other forms of sarcoidosis and may easily simulate if not actually develop into tuberculosis. Bronchiectasis and other chronic pulmonary conditions are not easily excluded except postmortem.

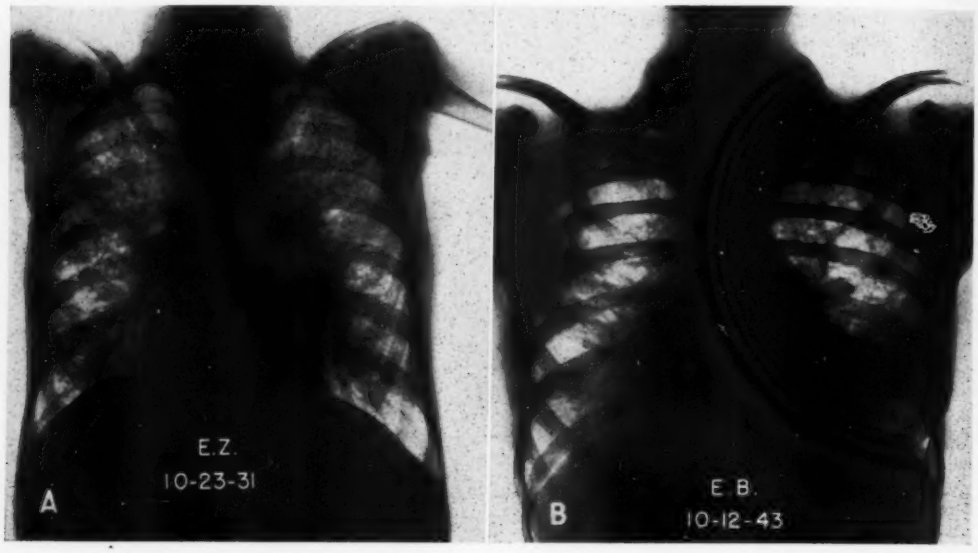

Fig. 7. Cases 10 and 11. Extensive confluent and submiliary infiltrations in diffuse sarcoidosis. In these cases, it is impossible from the roentgen appearance to determine whether other disease, such as tuberculosis or bronchiectasis, is present.

CASE 10: E. Z., a white male of 19 years, had been treated for so-called Hodgkin's disease and miliary tuberculosis at the age of 14. Marked hepatosplenomegaly and focal glomerulonephritis were present. Biopsy of a skin lesion revealed sarcoidosis. Calcific shadows in the right kidney were observed roentgenologically. X-ray study of the chest in June 1929 revealed diffuse infiltrations extending out from both hila which, at the periphery, had a miliary appearance. In October 1931 the infiltrations were more extensive and more confluent. They reached out from the hila in thick, dense strands. Some suggestion of fibrosis was present and in the right upper lobe there was an emphysematous, or possibly tuberculous, cavity (Fig. 7A).

CASE 11: E. B., a Negress of 26 years, complained of fever, cough, weakness, weight loss, and expectoration for five years. Skin lesions were present with persistent adenopathy. A diagnosis of tuberculosis had been made in Baltimore, although skin biopsies failed to show necrosis or caseation. On admission to the Mt. Sinai Hospital there were diffuse adenopathy, marked hepatosplenomegaly, a positive skin reaction to tuberculin, inversion of the globulin-albumin ratio in the blood serum, and an absence of tubercle bacilli in the sputum. Biopsy of axillary nodes revealed typical sarcoidosis. A chest roentgenogram in October 1943 disclosed confluent infiltrations in both lower lobes and in the lower part of the right upper lobe, with questionable areas of rarefaction and, at the left base, what appeared to be a small cavity (Fig. 7B).

COMMENT

Twelve cases of proved sarcoidosis have provided the basis for review of the more frequent thoracic manifestations of the disease which are demonstrable roentgenologically. Eight examples were selected for illustration. Chronicity and variable degrees of progression of lesions with a tendency to complete healing are stressed as prominent features. Hilar adenopathy and pulmonary infiltration of strand-like, reticulated, miliary, nodular, and confluent types are found. The recession of hilar adenopathy with extension of parenchymatous infiltrations and, *per contra*, enlargement of the hilar nodes with clearing of pulmonary infiltrations have been demonstrated. Although we have somewhat arbitrarily classified the roentgen features into five groups, following Leitner (6), these divisions are used only for description, as the disease changes constantly, and transition from one form to another is the rule.

Involvement of the heart, pericardium, or both is suggested by the changes in the size and shape of the cardiac shadow.

The resemblance roentgenologically between pulmonary sarcoidosis and other conditions, particularly tuberculosis, may be so close that a diagnosis from the chest roentgenogram alone is not justified. Biopsy, when possible, is the only satisfactory basis for diagnosis.

The discussion has been limited to the roentgen features of the disease. Consideration of the controversial subjects of etiology and relationship to tuberculosis has not been included.

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Roentgen Therapy of Mammary Carcinoma: Survival Study Based on 731 Cases[1]

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As early as 1500 B.C. carcinoma of the breast was treated by excision and by a variety of escharotics, including the Egyptian arsenical pastes. Hippocrates burned out carcinoma by cautery and, though the diagnosis was probably uncertain, this would seem to be the earliest record of destruction by heat.

Incidence: According to Hoffman (22) the number of women dying from cancer in Massachusetts from 1920 to 1929 was 146.6 per 100,000 population. In 1935, according to the U. S. Census, cancer of the breast caused 13,226 deaths, which was 9.29 per cent of the total cancer mortality of that year. Assuming that the patient with carcinoma of the breast lives about four to five years from the time when the cancer began to the time of death, Behan (9) estimates, on this basis, that about five times 13,000, or 65,000, women (in the United States) are sufferers from mammary cancer. Spackman and Hynes (45) state that it has been estimated that 2 per cent of women die from carcinoma of the breast.

Age (16): According to most writers, about 75 per cent of breast cancers are in women over forty, although no age beyond adolescence seems to be immune. Brewer reported a fibroadenoma with carcinomatous areas in a Negress of sixteen years. In elderly patients the course is usually slow, and fibrosis and cicatrization are prominent. Acute carcinosis is usually found in women under thirty-five, with well developed breasts.

Sex: Carcinoma of the male breast is of relatively infrequent occurrence. The incidence as given by most writers is from 0.3 to 0.5 per cent of all cancers of the breast. Sachs (40) reported on 205 cases of mammary carcinoma in the male collected from various sources; 178 of the cases were proved pathologically. On the basis of this series and others recorded in the literature, he gives the ratio of male breast cancer to female breast cancer as from 0.08 to 3.0 per cent, with a mean average of 1.16 per cent. In the series from the University of Minnesota Hospitals to be analyzed here, there were 3 males, 0.41 per cent of the total number of patients.

Heredity: Carcinoma of various organs has been reported as having a familial incidence in from 5 to 24 per cent of cases. Maude Slye (43) found that in mice selective breeding may ultimately produce strains in which different organs or systems will acquire a definite predisposition to certain types of malignant growth. Schreiner and Stenstrom (42) discovered a familial history of cancer in 133 (24 per cent) of 563 cases of breast carcinoma.

Lactation and Pregnancy: Earlier investigators (9) believed that carcinoma of the breast was more frequent in women who had not borne children. Ewing (16) believed that pregnancy was without definite influence. In experimental studies, however, it has been found that in certain strains of mice the spontaneous incidence of mammary gland tumors in breeding females a year old or over is between 80 and 90 per cent, whereas in virgin females of the same age and strain it is only 50 per cent (29).

Location: As to the exact site of mammary cancer, a slight predominance in

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the upper axillary segment of the left breast seems to have been established by statistical studies (16).

Trauma: Injury may accelerate the growth of a breast cancer, and traumatism has been asserted or suspected as a causative or predisposing factor in from 5 to 13 per cent of patients.

Estrogens: The role of estrogens in the etiology of mammary carcinoma is the subject of an editorial by Leucutia, who believes that the estrogenic theory is not without reasonable foundation. Injected estrogenic substances (4) will cause the growth of male mammary rudiments to such an extent that fatal mammary cancer may develop, and various clinical reports indicate that pregnancy increases the rate of growth of a pre-existing breast carcinoma. Pohle and Benson (37) expressed the opinion that "roentgen sterilization of all women, regardless of age, who have metastatic carcinoma from a primary carcinoma of the breast, and of all women of forty years or older operated on for breast cancer, should be recommended as a prophylactic measure." Taylor (46) observed that "carcinoma of the breast tended to metastasize earlier in young women than in older women, and that it tended to be of a higher grade of malignancy. Postoperative recurrence seemed to take place more promptly in younger women." In 20 of 50 patients in whom an artificial menopause was induced, 20 were said to show some possible or probable benefit, while striking improvement was observed in several instances. In conclusion, Taylor states: "We are confronted with a small subgroup of young women suffering from carcinoma of the breast in whom artificial menopause has shown striking benefit. It is suggested that the presence of the ovarian hormone in these cases is almost an essential condition for the growth of the carcinoma." Archer and Cooper (7) recorded a case in a married woman of thirty in which "a highly malignant and rapidly spreading carcinoma of the breast was observed not only to be held in check but to regress to an amazing degree" following induction of an artificial menopause. Thus, both experimental evidence and clinical observations tend to substantiate the theory that estrogenic substances accelerate the growth of mammary carcinomas and contribute to the production of early metastases.

CLASSIFICATION OF CARCINOMAS OF THE BREAST

Several classifications of neoplasms of the breast have been presented by various investigators. For this reason it is difficult to compare the reported results of therapy. It is important that, in comparison of statistical reports from different clinics and institutions, a universal criterion be adopted for the classification of cases. Schenck's modification of Steinthal's clinical grouping appears to be simple and adequate. Stage I includes those cases where the tumor is freely movable and is strictly confined to the affected breast; Stage II, cases with firm lymph nodes palpable in the axilla and a primary breast tumor usually exceeding 3 cm. in diameter, partially fixed to the skin and underlying tissues; Stage III, the edematous and inflammatory carcinomas, with a large mass involving a considerable portion of the mammary gland fixed to the skin and underlying structures, and adherent nodes in the axilla and the supraclavicular fossa or distant metastases; Stage IV, all recurrent carcinomas of the breast.

The classification of patients and the determination of operability are not easy. Kilgore (24) stated that "palpation of the axilla is notoriously inaccurate in identifying metastases. In fact, about 30 per cent of supposedly cancerous lymph nodes felt before operation are found to be innocent, while 40 per cent of patients considered free from axillary involvement prove on clinical examination to have metastases." He adds, however, that he has not seen a hard node more than 2 cm. in apparent diameter prove innocent, nor has he seen such a node unassociated with involvement of others. Lenz (25) found

that "even large axillary masses did not always contain cancer, as exemplified by 2 out of 13 patients with axillary masses 3 cm. in diameter and larger." We believe, however, that experienced examiners usually make few mistakes in classifying patients in the proper clinical groups.

An important item to include in a statistical analysis is the age incidence in the series under consideration. Though a definite variation of incidence in age groups has been observed, the age distribution is entirely omitted from some reports. This may lead to an erroneous impression of the results of roentgen therapy, since irradiation is of limited value in highly malignant breast cancers in younger women.

Another point which appears pertinent in a survival study is the actual cause of death. Most statistics are concerned with the length of life following surgery, irradiation, or both, without regard to whether the patient died free of carcinoma. It is difficult, of course, to obtain all pertinent information after a patient's death, and it is usually assumed that factors other than the breast cancer will, on an average, contribute to the same extent to the mortality in different series. This may not be true, particularly if the series are small. The majority of patients with carcinoma of the breast are in an age group in which hypertension, diabetes, cardiovascular, blood, renal, and other diseases are also common. We decided to avoid complication of the statistics by omitting consideration of the cause of death, as the number of patients in our series is relatively large.

METHODS OF TREATMENT

Thirty years ago carcinoma of the breast was treated almost exclusively by surgery. Today radical operation continues to be the method of choice generally, but evidence indicating the value of irradiation therapy has accumulated rapidly so that it is now commonly employed as a supplementary procedure. The use of roentgen rays in the treatment of carcinoma of the breast may be said to have begun in 1914, with the advent of the Coolidge tube, although as early as 1896 Emil Grubbe of Chicago treated a cancer of the breast with x-rays.

Technics and methods of treatment have changed and vary in many clinics today. To estimate the results of therapy on a statistical basis, therefore, is difficult (35, 49) and such conclusions are open to criticism. Pohle and Benson (37), Soiland (44), O'Brien (32), Spackman and Hynes (45), Pfahler (34), Schenck (41), Graham (18), Evans and Leucutia (15), Portmann (39), Bransfield and Castigliano (11), and numerous other authors have published survival statistics indicating that in mammary carcinoma of Stage II postoperative irradiation may increase the percentage of survivals from 10 to 25 per cent over surgery alone. Others (1, 8, 20, 21) have been pessimistic as to the value of irradiation in carcinoma of the breast, and have published statistics supporting their contentions. Adair (1) stated in 1943 that the improvement in survival "cannot be entirely attributed to the addition of irradiation." This same writer, however, in discussing (2) the paper by Spackman and Hynes on "Surgery and Irradiation in the Treatment of Cancer of the Breast," in 1938, reported that, in 200 patients with breast carcinoma who were subjected to preoperative irradiation, the surgical specimens as examined by Doctors Ewing and Stewart showed a total destruction of the primary tumor in 33 per cent and of the deposits in the axilla in 22 per cent.

Beach (8) reported on 5 patients preoperatively irradiated for carcinoma of the breast and stated that "careful histological study revealed persistence of the carcinoma in all of the cases," though a relatively high dosage had been administered and an adequate interval had elapsed for the full benefits of the irradiation to have taken place.

Harrington (20), reporting on surgical survival in carcinoma of the breast, stated in 1933 that "post-operative roentgen therapy is not a definite auxiliary to

surgical treatment. In selected cases in which the grade of malignancy is high it may be of value, but it is of no benefit if the grade of malignancy is low." In a later publication (21) he wrote: "The surgical results may be influenced by the use of roentgen rays and the effectiveness of the roentgenological treatment depends, to some extent, on the degree of malignancy." He concludes, however, that "roentgen therapy is of no definite aid in radical surgical treatment of carcinoma of the breast and the figures indicate that it may be detrimental to the results of surgical treatment in some cases." This conclusion is based upon a group of patients who presented no axillary nodal metastases at the time of operation, and who lived on an average of one year longer than a similar group of patients who were treated by surgery and irradiation. Harrington does not state by what method the patients were chosen for surgery and irradiation. It seems unjustifiable to subject Stage I patients with no axillary metastases to irradiation following radical mastectomy, as his own report (20) states that "71.2 per cent survived five years following operation, 52.9 per cent were living ten years, and 40.7 per cent fifteen years after operation." Harrington did not state how long after surgery irradiation therapy was given.

Pendergrass and Hodes (33), on the basis of their experiences with preoperative irradiation, "hesitate to recommend it routinely. The average duration of life in the group of patients who received pre- and postoperative irradiation was less than any other operated group." Soiland (44), on the other hand, reported a great deal of benefit from preoperative irradiation.

Adair has summarized the results obtained at Memorial Hospital, New York, with an intense series of x-ray therapy followed by radical mastectomy after a period of about three months. He found that this method gave poorer results than immediate radical mastectomy. This indicates that surgery should be performed promptly after irradiation. Our method calls for fourteen days of preoperative treatment followed by radical mastectomy after an interval of fourteen days.

The experience in the Cancer Institute of the University of Minnesota Hospitals with preoperative roentgen therapy is confined primarily to inoperable carcinoma of the breast. For this reason the number of patients treated in this manner was small, as only a few cases became operable after irradiation. Metastases were usually extensive, and both irradiation and surgery were utilized as palliative measures.

We agree with Portmann (38), who states in his discussion of Adair's (1) paper that irradiation "prolongs life and economic usefulness." Experimental data and uniform statistical survival reports, with all forms of treatment, are the only satisfactory criterion by which we can arrive at that method which will be of the greatest benefit.

Combined operation and irradiation is the method of treatment advocated by the majority of radiologists. It postulates thorough radical mastectomy followed by irradiation adequate to destroy all cancer cells in the bed of the tumor and surrounding tissues.

Radical operations (27) have become well standardized by skilled and experienced surgeons. The mammary gland, fascia, muscles, and axillary contents are removed *en masse*. Unfortunately, however, cancer of the breast is not confined within these limits, as is evidenced by the fact that the general average of surgical curability in Stage II carcinoma, on the basis of the five-year survival rate, is approximately only 30 per cent. This means that in 70 per cent of the cases the disease had extended beyond the possibility of surgical removal by the time operation was performed.

Preoperative irradiation is being used and advocated by several well known clinics on the basis that the most highly malignant cells will be destroyed or attenuated in their growth and spread. The objections to this procedure are: (1) the necessity of a biopsy, in most instances,

for a definite diagnosis, thus opening a possible channel for spread due to surgical manipulation; (2) the postponement of surgery, which gives the cells some additional time to become disseminated.

Some surgeons question the advisability of radical mastectomy and irradiation on the basis of morbidity. At some time or another we have all seen swollen, useless arms as a result of interference with the lymph and blood flow. This complication is due to scarification in the axilla following surgery, often with postoperative infection. Whether radiation makes this condition worse is debatable. The number of patients, however, who suffer from this complication is comparatively small, although no definite statistical reports have been published to show its frequency. It may also be caused by metastasis and it is difficult to decide which factor is most important.

Fibrosis of the lungs is another complication following irradiation of the breast area, but it occurs in only a small percentage of the treated cases and seldom leads to severe disability.

Roentgen-ray sterilization for carcinoma of the breast has been advocated by many radiologists and appears to be of value in women who have not reached the climacterium. It is, however, often difficult to determine whether such a procedure will be beneficial in a given case.

Because of the frequency of recurrence in all forms of malignant growth, regardless of response to surgery, irradiation, or their combination, it is recommended that every patient with carcinoma of the breast be under observation for many years and be carefully examined at stated intervals after treatment (6).

Under the heading, "Theoretical and Biological Considerations for Postoperative Irradiation," Pfahler (34) writes: "Local postoperative treatment is intended (1) to destroy any malignant cells that may have been transplanted during operation; (2) to destroy any microscopical remnant of cancerous tissue which the surgeon may have missed, and (3) to render the normal tissue more resistant to cancerous growth. Definite evidence of implantation is furnished by the observance of stitch hole recurrences. Other more frequent implantations probably occur under the skin flap."

For the best effect, the postoperative treatment should be started as soon as the patient's general condition and circumstances will permit, usually ten days to two weeks after operation, even though the wound is not entirely healed. Postoperative irradiation, if mild, does not interfere with healing, but the healing period may be prolonged if the doses are too large. We believe that early postoperative irradiation lessens the opportunity for carcinomatous remnants to become active lesions.

ANALYSIS OF BREAST CARCINOMA CASES FROM THE CANCER INSTITUTE, UNIVERSITY OF MINNESOTA HOSPITALS

We have analyzed the records of all the patients—a total of 731—who received irradiation therapy for carcinoma of the breast at the University of Minnesota Hospitals during the thirteen years, 1926 to 1938, taking the date of the first deep-roentgen-ray treatment as the beginning of the survival period. In most of the patients a radical mastectomy was performed; in a few, simple surgical removal of the breast preceded roentgen irradiation.

Cases treated in the last two years of the period covered by the report obviously would not qualify for five-year survival statistics. The entire group was included, however, in order that the report might be as complete as possible from the standpoint of symptoms and other pertinent factors.

We have been able to follow up to 1939 all except 18 patients (2.4 per cent) of the 731 treated. Some of the 18 who could not be traced at that time had been followed as long as six years. Untraced patients were considered in our statistical studies as dying from carcinoma of the breast following the last recorded information.

In some instances in this series the evidence on the records is insufficient for a definite pathological classification based on the grade system, as a considerable number of patients were referred for roentgen therapy by surgeons outside of the University Hospitals staff, and it was frequently impossible to ascertain the exact type and stage of the carcinoma. The patients who were operated upon at the University Hospitals were classified on the basis of the pathological examination of the axillary content, and Stage I cases did not, as a rule, receive radiation. It should be noted that these patients were operated upon by a great number of surgeons, among whom were many having limited experience. Because of uncertainty concerning Stages I and II, the patients have been simply grouped into three classes, as follows:

(1) Those referred for postoperative therapy, in whom the axillary nodes were supposedly involved at the time of operation and a radical mastectomy preceded irradiation by a reasonably short period. No recurrences or metastases were evident in this group at the beginning of irradiation. Since a few of these patients probably had no axillary lymph node involvement, this group includes Stages I and II (certainly not over 10 per cent in Stage I).

(2) Those patients with recurrences or metastases following either a simple palliative mastectomy or a radical mastectomy. In some of these patients, distant metastases were present but were not evident prior to operation.

(3) Inoperable cases, in which massive breast involvement existed, distant metastases were found on first examination, or the age or physical condition of the patient constituted a poor operative risk.

Sex and Age: Our series of cases of breast carcinoma included 728 females and 3 males. The patients were divided into age groups in one-half decades, so as to show the increase in incidence after the age of thirty-five years (Table I). Eighty-seven per cent were between the ages of thirty-five and seventy, and 85 per cent were over forty. The youngest patient was twenty-two years of age, and the oldest ninety-one.

TABLE I: AGE INCIDENCE BY HALF DECADES FOR 699 PATIENTS

Age	Cases	Per Cent
20–24	5	0.7
25–29	9	1.0
30–34	28	4.0
35–39	62	9.0
40–44	92	13.0
45–49	109	15.0
50–54	111	17.0
55–59	90	13.0
60–64	69	10.0
65–69	72	10.0
70–74	28	4.0
75–79	13	2.0
80–84	10	1.0
85–89	0	0.0
90–94	1	0.1

These figures indicate a definite increase of patients in the higher age group (85 per cent) over the figures given by most other authors, who report 75 per cent of their patients above the age of forty years. Lewis and Rienhoff (28) found 81 per cent in a series of 950 patients to be over forty years of age and Nathanson (30), reviewing a series of 2,165 cases, reports a peak incidence between forty-six and forty-eight years.

Symptoms and Duration: Of the 731 patients treated, 686 gave histories of symptoms such as pain, a mass, ulceration of the breast, discharge from the nipple, etc., with a fairly accurate date of onset. In the other patients, the onset of symptoms was very indefinite or was not recorded at all in the history.

TABLE II: DURATION OF SYMPTOMS

Duration	Cases	Per Cent
1 month or less	100	15
2–4 months	148	21
5–7 months	95	14
8–12 months	114	17
Over 1 year	229	33

One hundred patients (15 per cent) had symptoms for one month or less; 357 patients (52 per cent) for one month to one year, and the remaining 229 patients (33 per cent) for over a year (Table II).

RECENT COMPARATIVE STATISTICS OF RESULTS AS COLLECTED FROM SPECIAL CLINICS (PFAHLER)

Surgery Alone, Percentage Living 5 Years				Surgery and Postoperative Irradiation, Percentage Living 5 Years			
Author	No. of Cases	Stage II	All Operated Cases	Author	No. of Cases	Stage II	All Operated Cases
Harrington	1911	25.0	33.1	Westermark	70	38.0	37.0
Gould	151	22.0	33.1	Evans and Leucutia	175	46.3	46.1
Abell	217	36.0	46.0	Wintz	97	51.5	..
Redman	106	41.0	44.0	Lee	217	53.0	41.0
Jessop	216	30.5	48.0	Weisswang:	171	27.1	53.7
Klingenstein	..	17.0	23.0	Billich	164	..	39.6
Lewis and Rienhoff	420	..	18.0	Gäbel and Magens	..	33.3	47.7
Gask	..	..	36.0	Holfelder	118	..	50.0
				Webster	358	..	42.0
				Nicolson and Berman	74	..	36.8
				Hummel	115	..	68.7
				Pfahler and Vastine	269	52.0	52.4
				[Gratzek and Stenstrom	254	..	51.0]
Average percentage		27.9	35.0	Average percentage		39.6	46.8 [47.4]

The shortest admitted duration of symptoms was two weeks before roentgen irradiation, and three days before operation. The longest duration of symptoms was forty-two years, a breast tumor having been first noticed in the year 1890. Following trauma, the mass underwent malignant change with generalized metastasis at the time of death.

Classification of Patients: In Table III the patients are classified into the groups previously described. There were 324 patients (44 per cent) referred for postoperative prophylactic deep roentgen therapy; 292 patients (40 per cent) were treated for recurrent and metastatic disease; 115 patients (16 per cent) were inoperable.

TABLE III: CLASSIFICATION OF PATIENTS IN GROUPS, WITH NUMBER OF PATIENTS REFERRED FOR TREATMENT BY YEARS

Year	Postoperative Prophylactic Irradiation	Metastatic and Recurrent Cases	Inoperable Cases	Total
1	3	12	2	17
2	13	19	2	34
3	9	12	2	23
4	22	17	1	40
5	18	29	4	51
6	27	31	9	67
7	36	25	13	74
8	42	39	9	90
9	36	29	11	76
10	33	20	17	70
11	15	18	12	45
12	32	13	17	62
13	38	28	16	82
TOTAL	324 (44%)	292 (40%)	115 (16%)	731

Postoperative Prophylactic Irradiation: Table IV presents the results in 324 patients (44 per cent) treated prophylactically accompanying operation: 129 patients out of 254 (51 per cent) survived five years or more and 37 out of 128 (29 per cent) survived ten years or more. It is also of interest that 6 out of 16 patients were alive after fifteen years.

The accompanying table, taken from Pfahler's publication of 1938 (34) shows comparative percentages of five-year survival in Stage II carcinoma of the breast and in all operated cases with surgery alone and with surgery and irradiation combined. The figures in our series have been added and the average has been corrected accordingly (figures in brackets).

In a subsequent paper, appearing after the publication of Pfahler's table, Evans and Leucutia (15) reported a 50 per cent five-year survival in a series of patients with Stage I and II carcinoma of the breast, treated by surgery and roentgen therapy, and a 42 per cent 10-year survival. Wintz (48) found that 48 per cent of 124 patients with Stage I and II carcinomas of the breast survived five years.

Recurrent, Metastatic, and Inoperable Group: No radiologist pretends to claim a high percentage of cures in those un-

TABLE IV: SURVIVAL OF PATIENTS IN GROUP WITH CARCINOMA OF THE BREAST TREATED PROPHYLACTICALLY BY IRRADIATION FOLLOWING RADICAL MASTECTOMY
(Treated at University of Minnesota Hospitals from July 1, 1926, to Dec. 31, 1937)

Year	No. of Cases	Number of Years														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1926	3	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1
1927	13	12	9	7	7	7	7	5	5	5	5	5	5	5	5	5
1928	9	8	7	7	6	5	5	4	4	4	3	3	3	3		
1929	22	17	11	8	6	4	2	1	1	1	1	1	0			
1930	18	15	12	11	10	8	8	7	7	7	7	7				
1931	27	21	19	15	11	11	10	9	8	8	6					
1932	36	31	29	27	25	22	19	16	16	16	14					
1933	42	39	33	32	28	24	24	24	21							
1934	36	35	28	27	25	21	21	19								
1935	33	29	26	20	18	17	16	13								
1936	15	14	12	11	9	9										
1937	32	28	26	22	20											
1938	38	32	28	22												
TOTAL	324	324	324	324	286	254	239	239	170	128	128	65	47	25	16	16
Living		283	242	210	166	129	113	99	63	42	37	17	9	9	6	6
Percentage living		87	75	65	58	51	47	41	37	33	29					

TABLE V: SURVIVAL OF PATIENTS IN THE RECURRENT, METASTATIC, AND INOPERABLE GROUPS

Year	No. of Cases	Number of Years														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1926	14	10	6	4	2	2	2	2	2	1	0					
1927	21	8	5	3	2	2	2	2	2	2	2	1	1	1	1	1
1928	14	8	3	1	1	1	1	1	1	1	1	0				
1929	18	8	5	2	1	1	1	0								
1930	33	17	9	7	1	1	1	1	1	1	0					
1931	40	19	13	11	9	6	4	2	2	2	2	1				
1932	38	16	10	5	4	4	3	2	2	2	2	1				
1933	48	29	20	11	8	6	5	4	3	2						
1934	40	25	14	9	6	2	2	2								
1935	37	22	15	6	5	3	2									
1936	30	15	5	3	1	1										
1937	30	18	8	6	5											
1938	44	28	17	8												
TOTAL	407	407	407	407	363	333	303	266	226	178	178	178	67	49	35	35
Living		223	130	76	45	29	23	16	13	9	7	3	1	1	1	1
Percentage living		55	32	18	12	9	7	6	6	5	4	2				

fortunate persons who have postoperative carcinomatous recurrences, metastases in the bones or elsewhere, or who are otherwise inoperable. Many extremely painful metastases, however, have responded so well to roentgen therapy that bedridden patients have been able to resume their household duties for months, with freedom from pain and other discomfort. Some inoperable patients have become operable following therapy, and in others recurrences have subsided satisfactorily (31).

Table V covers 407 patients (56 per cent of the total of 731) treated for recurrent, metastatic, or inoperable cancer. Of these, 223 (55 per cent) survived one year or more; 76 (18 per cent) survived three years; 29 (9 per cent) out of 333 treated survived five years, and 7 out of 178 (4 per cent) ten years. One patient was alive fifteen years after treatment.

Among the 9 patients who survived ten years or more, there may be a few in whom metastases were incorrectly diagnosed, but in some of the group metastatic lesions were undoubtedly controlled for that peroid. The following is the history of a patient who was considered inoperable.

CASE HISTORY: An unmarried woman aged 45 years was referred to the University Hospitals on Dec. 22, 1933, having been aware of three lumps in her right breast and one in her left breast since 1908 (twenty-five years). She had been in the University Hospitals Out-Patient Clinic in 1913

(five years after onset) but because of the multiplicity of the nodules was advised to leave them alone, as the condition was considered benign. No biopsy was done. About October 1933 (twenty years following the first examination), the patient noticed a new "string of lumps" medially in her right breast, and on Dec. 7, she consulted a physician, who referred her to the University Hospitals.

Physical examination revealed multiple masses in the right breast with right axillary and right supraclavicular palpable nodes. One mass was present in the medial side of the left breast and a node was palpable in the left axilla. A few of the masses in the right breast were attached to the skin, and some of these were excised by diathermy on Dec. 23, 1933. Microscopic study revealed scirrhous carcinoma. On Dec. 28, radon implants (49.3 mc.) were inserted into the right breast, right axilla, and right supraclavicular regions for a total dose of 6,720 mc.-hr. During May 1934 the patient received 1,000 r (measured in air) deep roentgen therapy to the right breast, right axilla, and right supraclavicular areas, with 200 r added in the latter two regions. She was followed in the Out-Patient Tumor Clinic up to June 1937, and on Oct. 6, 1943, she was working and apparently well. It is probable that she had a benign lesion in the left breast with an inflammatory adenopathy in the left axilla, as these areas have remained dormant without any type of therapy.

This patient has so far survived almost ten years without recurrence, though no radical surgery was performed and roentgen irradiation and radon implantation were the main forms of therapy given.

Subdividing the patients into those with recurrences and metastases and those who were inoperable, we find that 292 (40 per cent of the entire group of 731) were treated for recurrent and metastatic carcinoma. There was a three-year survival of 51 (17 per cent) out of 292 patients treated, while 21 (8 per cent) out of 251 treated survived five years (Table VI).

TABLE VI: SURVIVAL OF PATIENTS WITH RECURRENT AND METASTATIC CARCINOMA OF THE BREAST

Years	Number Treated	Number Surviving	Per Cent Survival
1	292	165	57
2	292	90	31
3	292	51	17
4	264	29	11
5	251	21	8
6	233	16	7
7	213	11	5
8	184	9	5
9	145	7	5
10	120	4	3
11	89	1	
12	60	1	

The 115 patients considered to be inoperable and referred for therapy are considered in Table VII. As was previously explained, these patients were considered inoperable because of acute carcinomatous involvement, an extensive local lesion and metastases, or because of being poor surgical risks. We find that 58 patients of the 115 treated (50 per cent) survived one year, 25 out of 115 patients treated (22 per cent) survived three years, and 8 patients out of 82 treated (10 per cent) survived five years.

TABLE VII: SURVIVAL OF PATIENTS WITH PRIMARY INOPERABLE CARCINOMA OF THE BREAST

Years	Number Treated	Number Surviving	Per Cent Survival
1	115	58	50
2	115	40	35
3	115	25	22
4	99	16	16
5	82	8	10
6	70	7	10
7	53	5	9
8	42	4	9
9	33	2	6
10	33	2	6
11	33	2	6
12	7	0	

A few of the patients became operable after an intense series of roentgen therapy, but they have been included in this group as they were definitely inoperable to start with and the later operation was considered as palliative only.

Survival of Entire Group: Unfortunately we do not have a follow-up on all patients with carcinoma of the breast who came to the Clinic. Some of these patients were treated by surgery alone, and the survival in this group was high, as it was made up of Stage I cases. As we have accepted all patients desiring palliative treatment, only a few persons with extensive metastases failed to receive x-ray therapy, either because they refused such treatment or because they had no complaints except from advanced pulmonary metastases. The survivals for all treated patients, independent of the extent of the disease, are summarized in Table VIII.

It is noticeable that, when no consideration as to the stage of the disease is given,

TABLE VIII: SURVIVAL IN ALL CLINICAL GROUPS OF CARCINOMA OF THE BREAST TREATED BY IRRADIATION ALONE OR IN COMBINATION WITH SURGERY
(Most of Stage I cases excluded)

Years	Number Treated	Number Surviving	Per cent Survival
1	731	506	69
2	731	372	51
3	731	286	39
4	649	211	33
5	587	158	27
6	542	136	25
7	542	116	21
8	396	76	19
9	306	51	17
10	306	44	14
11	165	18	10
12	114	10	9

we have a 27 per cent five-year survival, based on a total of 587 patients treated, and a ten-year survival of 14 per cent, based on a total of 306 patients treated. No satisfactory comparison can be made with figures given by other authors, as the selection of cases differs and as Stage I cases were selectively excluded in our series. It is interesting, however, to recall that Evans and Leucutia (15) report 30 per cent five-year survivals among 830 cases treated, and 22 per cent ten-year survivals based on 434 cases. In Lewis and Rienhoff's (28) combined series of medullary, scirrhous, and adenocarcinomas, 23 per cent of the patients survived five years.

Metastases and Recurrences: Among the entire group of patients with records specifying the presence of metastases, the axillary and supraclavicular nodes, bones, and lungs predominate as the sites of secondary involvement. Bell (10) stated that over two-thirds of the cases show axillary metastases at the time of operation, while Trimble (47) stated that, in 80 per cent of the patients presenting themselves for examination because of a lump in the breast, metastases have already occurred. Lewis and Rienhoff (28) substantiate our observations that usually the younger the patient with carcinoma of the breast, the more susceptible she is to local or axillary recurrences.

Table IX shows the incidence of metastases for different regions and of local or axillary recurrences. The heading "other regions" includes such sites as the omentum, intestines, peritoneum, the genito-urinary system, inguinal nodes, etc., and instances specified in the records as "generalized metastases." These figures include metastases to more than one region in the same patient where mention of these is made in the record. This list cannot be considered complete but gives some information concerning the relative frequency of metastasis to different organs or locations.

TABLE IX: SITE OF METASTASES FROM CARCINOMA OF THE BREAST

Site	Numerical Incidence
Local recurrence	54
Axillae (recurrence)	225
Supraclavicular nodes	78
Other breast	20
Lung	77
Bone	148
Skin	41
Liver	25
Brain	11
Adrenal	1
Other regions	127

In one instance metastases were found in the adrenals. The history in this unusual case is as follows:

CASE HISTORY: A 69-year-old white female was admitted to the University Hospitals in December 1923, complaining of pain, swelling, and blue discoloration of the left breast, occurring after a fall (Nov. 23, 1923) in which the breast was injured, with subsequent development of a mass in the upper outer quadrant. Examination revealed a mass about 4 cm. in diameter and palpable left axillary nodes. A radical left mastectomy was done on Dec. 5, and a microscopic diagnosis of scirrhous carcinoma with axillary node metastases was made. The patient made an uneventful recovery and was discharged. A roentgenogram of the chest was negative. On Feb. 21, 1927, three years later, the patient was readmitted, complaining of a lump in the left axilla which she had first noticed two weeks previously. She had a brownish discoloration of the face, neck, and hands, which had been increasing, and a small ulcer on her right forearm, which would not heal. Roentgen examinations of the gastro-intestinal tract were negative. A diagnosis of one staff physician was "acanthosis nigricans," while a dermatologist suggested "pseudopellagra," a condition occasionally seen in association with malignant growth. Four deep roentgen ther-

apy treatments were given, amounting to 800 r (measured in air) to the left breast region and 1,000 r to the left axillary region. The patient died on March 20, 1927, on the 27th hospital day.

The autopsy report described the yellowish-brown pigmentation of the skin as more intense on the exposed regions, with scaling and thickening in those parts. There was a dark brown blotchy pigmentation of the mucous membranes of the mouth. The lungs, liver, spleen, myocardium, stomach, intestines, and right kidney were normal. The upper pole of the left kidney and both adrenals were entirely replaced by metastatic scirrhous carcinoma.

This was a case of Addison's disease due to bilateral metastatic carcinoma of the adrenals with no other organs involved, except the upper pole of the left kidney, by extension.

Bilateral Breast Carcinoma: It is of some interest to analyze the results in patients with carcinoma of both breasts. Of the 731 patients, 9 (1.2 per cent) were found to have bilateral breast carcinoma on first examination. Eight others received treatment for carcinoma of the second breast at a later date. In a few carcinoma of the second breast may have developed after they were last examined here, as seems to be the case with one patient who stated in a letter to us that she had cancer of the other breast but considered it useless to return for further treatments. Several patients had tumors of the second breast which were either proved to be benign or could not definitely be considered carcinoma. Some authors (18) report a much higher incidence of bilateral breast carcinoma, even up to 51 per cent of their cases, but in most instances only 1.5 per cent of primary bilateral involvement.

Three of the patients with primary bilateral carcinoma had bilateral radical mastectomy. Two of them survived more than one but less than two years; the third died within a year after operation. One patient had a bilateral simple mastectomy and lived for one year. The other 5 patients were considered inoperable and received radiation therapy only. Four died within one year and the fifth three years and a half after the first treatment.

Of the 8 patients with later involvement of the second breast, 4 had bilateral mastectomy. The survival after the first and second operation, respectively, was as follows: Case 1, 3 and 0 years; Case 2, 8 and 4 years; Case 3, 12 and 9 years; Case 4, 13 and 11 years. The latter two patients were alive and well in June 1943. Four patients had mastectomy for the original growth but were considered inoperable when they came to the clinic with involvement of the second breast. The survival from the time of operation and from first x-ray treatment to the second breast was: for two cases 1 and 0 years, for one 2 and 1 years, and for one 3 and 1 years.

These results indicate an exceedingly poor prognosis for primary bilateral breast carcinoma and in such cases radical mastectomy appears of little value. On the other hand, when a carcinoma of the second breast occurs at a subsequent date and is definitely operable, radical mastectomy should be performed and postoperative roentgen therapy given. In this group 2 out of 4 patients survived more than nine years. This seems to indicate that the second carcinoma was a new, independent growth rather than a metastatic lesion.

CASE HISTORY: A 41-year-old married female was first admitted to the University Hospitals in January 1930 She had noticed a mass in her left breast since 1912, which was biopsied at that time and found to be a benign lesion. In November 1929 (seventeen years later) pain and swelling occurred in the old biopsy scar. On Jan. 7, 1930, a radical mastectomy was performed and a microscopic diagnosis of adenocarcinoma was recorded. Axillary nodes were reported not involved. The patient was referred for roentgen therapy in February 1930, and 1,000 r (measured in air) were given to the left breast, left axilla, and left supraclavicular regions over a twelve-day period. There were no recurrences and no metastases up to May 1932 (two and a half years after the primary left breast lesion), when a mass was discovered in the right breast. A radical right mastectomy was performed on May 26, 1932. A pathological diagnosis of carcinoma was made, but whether any nodes were involved was not recorded. In June 1932 the patient was referred for deep x-ray therapy and was given 1,000 r (measured in air) to the right breast region with 400 r added to the axilla and supraclavicular regions; a similar series was given in August 1932. This patient survived for thirteen and eleven years, respectively, after carcinoma of the left and right breasts and, when heard from recently, was still well.

Tumors with Short History: In our analysis as to duration of symptoms before the institution of any therapy, 100 patients were found to have reported symptoms of one month or less. The information obtained was satisfactory enough in 79 cases to include them in a separate analysis. Forty-three of these patients came to the clinic before receiving any treatment, and 34 came with recurrences following mastectomy. It is of interest that in most of the latter patients recurrence developed relatively soon after the operation. The survivals following radiation therapy for the recurrent lesions were also relatively short, and it seems that the majority of these patients had highly malignant tumors. It was evidently rapid growth of the tumor and discomfort that brought them to a physician so soon after the discovery of the original mass. The same reason brought several of the first mentioned group to the clinic, as evidenced by 6 patients who were considered inoperable either because of metastasis or because of an inflammatory type of carcinoma. The results from surgery and irradiation in the operable cases were, however, better than usual, as the five- and ten-year survivals amounted to 60 per cent and 36 per cent, respectively. Because of the small number of patients, however, these figures are not significant. There can be no doubt that much better results would be obtained in the entire group of breast cancers if the patients came for operation immediately upon discovery of the tumor, though even under such circumstances there will undoubtedly be some who already have distant metastases.

Some investigators (28) have found that, in instances where medical care is sought very early after an abnormal growth or ulceration is noticed, the condition frequently is of an acute nature, progressing rapidly. For that reason, the patient becomes alarmed and requests aid promptly but the lesion proves to be of such a malignant nature that even the best and most thorough treatment is of little or no avail.

TECHNIC OF THERAPY

1. Postoperative Prophylactic Irradiation: Prophylactic therapy was usually started about ten to fourteen days following operation, with the following factors: 200 kv.p., 30 ma., 0.5 mm. Cu and 1.0 mm. Al filter (H.V.L. 0.9 mm. Cu), focal skin distance 70 cm. The field included the anterior breast region, anterior supraclavicular, cervical and axillary regions, and the parasternal line medially. At first about 250 r (in air) was given every second day for four treatments (total 1,000 r). The intention was to repeat this series after two months, but some of the patients did not return at that time. Since 1928 additional treatments have been given to the axilla and the supraclavicular region. The dose was gradually increased to some extent and co-operation improved so that practically all patients received the dose originally planned. With these changes the results improved: 36 of the 92 patients treated from 1926 to 1931 (39 per cent) survived five years, whereas 93 of the 162 patients treated from 1932 to 1936 (57 per cent) showed a five-year survival.

At the present time 140 kv.p., with 1.0 mm. Al and 0.25 mm. Cu filtration (H.V.L. 0.56 mm. Cu), are used for the large field at 70 cm. target-skin distance. The full series is given over a period of fourteen to sixteen days. During that time the above field receives 1,200 r (in air). The axilla and the supraclavicular areas receive, in addition, 300 r anteriorly and 1,200 r through posterior fields, with 200 kv., 1.0 mm. Al and 0.5 mm. Cu filter (H.V.L. 0.9 mm. Cu), and the breast area receives additional radiation from two tangential fields, 300 r being delivered to each. No statistics are as yet available for this method.

Most women in the menstrual period of life are urged to have permanent sterilization doses of deep roentgen therapy to the ovaries, being required to sign permission for sterilization before this is given.

2. Recurrent and Metastatic Cases: Every such case had to be individualized

from the standpoint of therapy, and the amount of radiation was largely a matter of personal judgment on the part of the therapist.

3. Inoperable Cases: In this group of patients the involved breast was treated in quadrants, with the beam directed tangentially through the breast. The breast is divided into a superior, inferior, medial, and lateral triangular quadrant, and the patient placed in such a position as to minimize the amount of radiation striking the lung parenchyma. The anterior supraclavicular region is included in the upper breast quadrant and the axilla in the lateral quadrant. Each field was treated by a fractional dose method so that at the conclusion of treatment, between 1,000 r and 1,500 r (measured in air) had been given per field, with 200 r to 300 r (measured in air) as the maximum daily dose to one quadrant. The posterior axilla and posterior supraclavicular areas received supplementary treatment with 600 to 900 r each. The factors used were 200 kv.p., 30 ma., 60 cm. focal skin distance, 1.0 mm. Al and 0.5 mm. Cu filtration (H.V.L. 0.9 mm. Cu), with 46.4 r per minute as the output. Where indicated, a permanent sterilization dose of therapy was given to each patient who did not object to it.

Complications and Sequelae: Occasionally patients complained of irradiation sickness. This usually had no great significance. If it were severe, the usual dosage was diminished until the condition improved. Some of the late sequelae were lung fibrosis as a result of radiation penetrating the pleura and lung parenchyma and causing a pleuropulmonitis, as described by Desjardins (14) in 1926. Skin reactions occur rarely, and usually subside promptly after a discontinuance of therapy. Occasionally permanent telangiectasia was observed as a late sequela.

SUMMARY

1. In this analysis the period of survival is considered from the day of the first roentgen treatment.

2. Seven hundred and thirty-one patients were treated by deep roentgen therapy for carcinoma of the breast, 728 females and 3 males.

3. Eighty-five per cent of the patients were above the age of forty years.

4. Four hundred and fifty-seven patients (66 per cent) had symptoms of one year or less.

5. Three hundred and twenty-four (44 per cent) received postoperative prophylactic therapy, with a three-year survival of 210 (65 per cent), a five-year survival of 129 patients out of 254 treated (51 per cent), and a 10-year survival of 37 out of 128 treated (29 per cent).

6. Four hundred and seven (56 per cent) were treated for recurrent, metastatic, and inoperable lesions, with a one-year survival of 223 (55 per cent); 76 patients surviving three years (18 per cent); 29 patients out of 333 treated surviving five years (9 per cent), and 7 out of 178 (4 per cent) surviving ten years.

7. Metastases were most common in axillary nodes, bones, the supraclavicular region, and lungs.

8. Early diagnosis and immediate irradiation therapy following radical mastectomy gave the best results.

9. Lung fibrosis as a complication can be minimized if a suitable technic is selected and fields are properly rotated.

CONCLUSIONS

Carcinoma of the breast is still a cause of death in a high percentage of the population. Early diagnosis, with immediate radical surgery followed by adequate deep roentgen-ray therapy, or operation preceded by irradiation, produces the most favorable results known today. Statistics from various clinics show a much higher percentage of five- and ten-year survivals with this combination than with surgery alone in Stage II carcinoma of the breast.

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Roentgen Therapy in Diseases of the Blood-Forming Organs[1]

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WHILE ROENTGEN therapy is recognized as the best symptomatic treatment available for leukemia, Hodgkin's disease, and similar conditions, there is apparently no standard method of irradiation. The details appear to differ in some respects with each roentgenologist. The present study was undertaken to determine the actual results of treatment and, if possible, to account for the remarkable difference in the outcome in different patients. The physician tells the roentgenologist: "This patient has leukemia" (or Hodgkin's disease, or some related condition) and asks: "Will you treat him?". The resultant treatments are of many types.

The case histories of 980 patients with diseases of the blood and blood-forming organs, receiving roentgen therapy, were reviewed to note the effect of different factors on the results. The diseases included various stages of myelogenous, lymphatic, monocytic, and atypical-cell leukemias, types of Hodgkin's disease, and lymphosarcoma. Statistical data will be published in another paper, but certain results of the analyses are given here, with case reports illustrating the essential points.

The x-ray therapy received by these patients represented the current practice of roentgenologists from numerous sections of the country, many of the patients having been treated in other clinics and hospitals before they were examined by us. Treatments were of many types, and it was extremely difficult to compare the effects of similar doses, whether stated simply as the number of roentgens or with all the technical factors. There appears to be no way at present of representing what was done to one patient in terms in any way comparable to what was done to another. From the state of the patient, his blood, or other factors, it was impossible to predict from a study of the records what a given series of x-ray treatments would do, as the technics were so varied. Some excellent remissions were recorded, whereas in other patients an exacerbation of the disease process resulted.

In actual practice, remissions last for varying times, from days to months. It is of practical importance to note what factors in the treatment or the condition of the patient influence their length and degree. Among the variable factors which could be analyzed were: stage of the disease (duration to the present time), the leukocyte count, maturity of the cells in the blood, maturity of the cells in the marrow, red blood cell count, platelet number, tendency to bleed, fever, age of patient, sex, number of previous relapses, previous treatment (irradiation), kinds of accessory treatment, lymphocyte count, basal metabolic rate, total "dosage" of x-ray (r), method of application, frequency of exposure, number of days in which treatment was given, parts irradiated, and size of field.

In analyzing the effects of treatment the following factors were taken into consideration: symptomatic remission, temperature decrease, increase or decrease in the leukocytes, increase or decrease in red cell count, platelet number, length of remission, change in weight, basal metabolic rate, pulse rate, uric acid output, chemical changes, bone marrow changes, peripheral blood changes, and re-establishment of the menstrual periods.

INTERVAL OF DOSAGE

In the following case of chronic myelogenous leukemia a comparison is made between giving doses of 200 r on alternate days (total 1,600 r in sixteen days) and

[1] Read by title at the Twenty-ninth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1–2, 1943.

giving 800 r on three consecutive days and one exposure three days later (same technical details of dosage). (This last dose should have been grouped with the others.) No demonstrable remission was produced in the first series, but a remission of about three months followed the second series. These two types of dosage interval were encountered frequently in the series of patients with results very much like those shown in this patient. Case II illustrates the short remissions when the alternate day interval is used.

CASE I: Man, age 38 years. Chronic myelogenous leukemia. Treatments over the spleen area. The blood counts on any given day were taken before the treatments were given. They were as follows:

Day	Leukocytes per Cu. Mm.	X-ray Irradiation to Spleen Region
−5	222,600	...
−4	161,600	...
−3	172,200	...
−2	157,000	...
−1	284,400	...
0	239,200	200 r
1	238,800	...
2	216,600	200 r
3	175,800	...
4	192,800	200 r
5	183,800	...
6	204,600	...
7	155,400	200 r
8	152,000	...
9	124,000	200 r
10	132,200	...
11	118,200	...
12	134,200	200 r
13	129,200	...
14	168,000	200 r
15	102,600	...
16	150,400	200 r
17	100,800	...
18	121,000	...
19	96,800	...
20	103,600	...
21	79,600	...
22	148,400	...
23	115,800	...
24	83,000	...
25	134,000	...
26	128,000	...
27	134,000	...
28	150,400	200 r
29	103,400	200 r
30	140,600	200 r
31	91,800	...
32	122,000	...
33	103,800	200 r
34	66,200	...
35	77,000	...
36	75,200	...
	Interval of 95 days	
131	224,400	...
132	276,200	...
133	249,200	...

SIZE OF THE FIELD IRRADIATED

With the same technical factors, variation in the size of the field (area of skin exposed) appears to be important. Thus 200 r over a large field produces a much greater effect than the same number of units over a small area. This is especially evident when fields of two sizes are used on the same patient at different times. It is, of course, shown quite well when adequate "spray" technic is used as compared to a limited area.

AREA EXPOSED. CHEST AND SPLEEN REGION: EFFECT OF TOO SMALL A DOSE

A relapse may be instituted if a small dose of x-ray is given or if it is given over an area where it affects much of the bone marrow directly.

CASE II: Man, age 34 years. Chronic myelogenous leukemia. The patient had a severe paroxysmal cough, which did not respond to sedatives or cough medicines of any type. His leukocyte count was 15,400 per cu. mm. with most of the cells of fairly mature types. He was treated over the anterior surface of the chest, through a 15 × 15-cm. field, and later over the spleen (10 × 5 cm.). The leukocyte changes are shown in the following table. At the beginning of the treatment the patient was in a remission induced by Fowler's solution.

Day	Dose in r	Leukocyte Count	Area Exposed
1	35	15,400	Chest
4	50	14,500	Chest
11	50	17,500	Chest
12	60	19,500	Chest
16	50	18,000	Chest
22	..	21,000	...
	Interval of 27 days		
49	..	255,000	...
54	75	175,000	Spleen
57	75	146,000	Spleen
61	..	54,000	...
70	..	21,400	...
	Interval of 26 days		
96	..	226,000	...
103	..	261,000	...
104	75	...	Spleen
106	75	206,000	Spleen
109	75	155,000	Spleen
113	75	90,000	Spleen
120	..	32,500	...
	Interval of 19 days		
139	..	141,000	Fowler's solution
153	..	136,000	...
181	..	76,600	...

Day	Dose in r	Leukocyte Count	Area Exposed
		Interval of 174 days	
355	..	72,800	...
363	50	80,000	Chest 15 × 15 cm.
366	70	52,200	...
369	70	60,000	...
371	90	100,000	...
376	100	203,000	...
378	100	288,000	...
380	30 spray	352,000	...
383	..	237,000	...
411	..	352,000	...

No great change in the leukocyte count was noted during the treatment over the chest, the white blood cell count during this period being but slightly above normal. A complete relapse followed, however, during the next four weeks. Here, comparatively "small" doses were given, not on consecutive days (five exposures in sixteen days, total 245 r). Two exposures over the spleen (not on consecutive days, 150 r in three days) caused a reduction to 21,400 leukocytes thirteen days later, followed by a complete relapse within the next three weeks. Four more treatments over the spleen (during nine days, total 300 r) reduced the leukocyte count to 32,500 in two weeks, but there was again a complete relapse in nineteen days. A remission was produced and maintained for eight months by the use of Fowler's solution.

As the patient's cough was severe, it was decided to try more x-ray therapy over the chest. The leukocyte count at this time was 72,800, the cells were mostly metamyelocytes, young and mature neutrophils, and from a hematological point of view the blood was in a comparatively good condition. Seven x-ray treatments were given at three-day intervals over seventeen days (total 510 r) and a complete relapse followed.

This patient should have responded perfectly to adequate treatment with x-rays as he did with Fowler's solution. His blood cells were in stages known to respond best to roentgen therapy, but the results were those of "stimulation" rather than depression.

PRODUCTION OF LEUKOPENIA

There is apparently no permanent harm if leukopenia is produced after x-ray therapy in chronic myelogenous leukemia. There may, however, be a prolonged reduction of the number of the red blood cells, white blood cells, or platelets, varying in different patients.

CASE III: Man, age 38 years. Myelogenous leukemia. The leukocyte counts in this patient were as follows:

Day	Leukocyte Count	X-ray (Spleen Area, Anterior and Posterior)
−4	152,400	...
0	...	200 r
1	...	200 r
2	...	200 r
3	...	200 r
4	...	200 r
10	125,200	...
16	184,000	300 r
17	191,000	300 r
18	166,500	...
19	109,000	...
20	78,800	...
27	28,300	...
31	14,800	...
35	9,300	...
42	5,800	...
45	3,800	...
48	5,900	...
52	2,900	...
56	3,000	...
63	5,100	...
70	8,600	...
73	23,700	...
	Remission for over eight months	

The depression in the leukocyte count lasted three weeks. There was a mild depression of the red cell count after the first five treatments, and again from the thirty-fifth to the fifty-sixth day. The platelets, which had been increased in number before therapy, were reduced in number after the fifth day and did not recover for about two months, reaching a low normal after that, with occasional periods of depression.

APLASIA OF RED BLOOD CELLS AND LYMPHOCYTES

CASE IV: A man, age 49 years, felt well until about two weeks before he came to us for examination. At another hospital it had been noted that he was pale and weak and had a mild fever. A biopsy section of a lymph node was interpreted there as a malignant tumor, a reticulum-cell sarcoma or metastatic carcinoma. (The disease was reticulum-cell sarcoma or "Hodgkin's sarcoma.") In the preceding eleven days he had received roentgen therapy, 1,850 r, over the inguinal, axillary, and left supraclavicular regions. This treatment proved quite toxic and the lymphocytes decreased to 440 per cu. mm. on the last day of the treatment, falling to 53 per cu. mm. during the next six weeks. The red blood cells decreased somewhat more slowly, but reached 1,800,000 in four weeks. The neutrophils did not decrease proportionately, but reached their lowest point in about the same time (1,350 per cu. mm.). A study of the bone marrow cells showed almost complete aplasia of the red blood cells, but a fair amount of neutrophilic leukocyte material remained. Improvement in the leukocyte count (lowest point, 2,000 per cu. mm. four weeks after the treatments) and in the red cell count followed blood transfusions, but the lymphocytes did not recover.

The blood platelets, increased in number at first, as is characteristic of Hodgkin's disease, became slightly reduced in number, and eventually recovered. Peritonitis developed from a ruptured duodenal ulcer, and a characteristic polymorphonuclear leukocytosis (neutrophils, 93 per cent of 19,200) occurred.

This case illustrates the fallacy of treating the disease rather than the patient. It shows the order in which toxic effects on the cells become evident and the order of recovery, when the lymph node areas are irradiated. Under the circumstances, the platelets resisted the treatment more than the other blood cells.

STATUS OF THE PERIPHERAL BLOOD AND THE BLOOD-FORMING TISSUES

The height of the leukocyte count in the peripheral blood and the degree of the maturity of the cells were factors in determining the effect of the treatments only to the extent that they represented the true status of the marrow, lymph nodes, or spleen. This is, of course, evident in the aleukemic forms, where the blood-forming tissues are hyperplastic and the peripheral blood shows a normal or leukopenic state. However, in patients with elevated leukocyte counts, the marrow at times harbored extensive nests of blasts while the peripheral blood showed comparatively few. In these cases, treatment with x-rays produced a poor or short remission, followed by an exacerbation. In such cases the number of blasts in the blood usually increased after irradiation, with progressive anemia. Frequently, when blasts formed about 5 per cent of the peripheral cells, the prognosis was uncertain, but when the percentage rose to 10 or higher, the effect of irradiation was either transient or deleterious. There was some suggestion that blood transfusion improved the prognosis in many cases that otherwise would have been expected to show a poor response. As a rule, the patient had a better chance of a remission when the blood cells were metamyelocytes or older in myelogenous leukemia, small lymphocytes in lymphatic leukemia, and young or mature monocytes in monocytic leukemia, than when the cells were younger, unless too frequent small doses of x-ray were given over long intervals.

RED BLOOD CELL AND PLATELET COUNT

A low red blood cell or platelet count was not in itself a prognostic factor in treatment. When the red blood cell tissue was active in the marrow, but crowded, improvement followed adequate reduction in leukocyte tissue following irradiation. A temporary fall in the red cell count was noted frequently after x-ray therapy by several of the different methods. This may have been the result of injury of the red blood cell tissue by the x-rays, or it may have reflected the increased rate of growth of the marrow (leukocyte tissue), which constituted the first change after irradiation, before the reduction started. In patients with adequate red blood cell growth (no room to mature beyond the normoblast stage), anemia was not a contraindication to x-ray therapy. When red blood cell tissue was depressed (acute leukemia: "blast" leukemia) x-ray irradiation caused a further anemia and was definitely contraindicated. It was evidently very difficult in many cases to evaluate this from the blood films alone, whereas in others it was quite obvious.

The platelet number in the peripheral blood did not, in itself, serve as a direct guide to treatment. Reduction in the platelet number was a contraindication to therapy only when accompanied by many leukocyte blasts in the peripheral blood. Many patients with chronic lymphatic leukemia and platelet reduction with anemia responded well to therapy. Failure in the manufacture of platelets was a definite contraindication to irradiation.

BASAL METABOLIC RATE

As a rule, the degree of activity of the leukemic process was reflected in the elevation of the basal metabolic rate. A simple clinical guide was the elevated pulse rate, but irritability, excessive perspiration, and loss of weight were other evidences. In those patients with fairly

mature cells in the blood and blood-forming organs, the high basal metabolic rate was an adequate guide for x-ray therapy, as the increased use of oxygen represented the degree of activity of the leukemic process. When many blasts were present, however, the basal metabolic rate alone was not an adequate guide.

AGE AND SEX

From the present analysis, it is not possible to formulate a definite statement as to whether an older or a younger person with the same degree of leukemic involvement responds better to x-ray therapy. The extremely wide range of responses may have been related to the many methods of irradiation. The problem will bear further study. Excellent remissions as well as poor ones were encountered in both young and old and male and female, with comparable conditions of the blood.

FEVER

An analysis of the case histories indicated that fever in itself was not a contraindication to x-ray therapy. The degree of advancement of the leukemia and the degree of immaturity of the cells were more potent factors, when accompanied by fever, than the mere elevation of the temperature. As a rule, extremely high temperatures (104–106°) accompanied conditions which in themselves would have ruled out x-ray therapy.

FIRST AND SUBSEQUENT REMISSIONS

An analysis of the cases shows that a second remission induced by roentgen therapy may be as long as the first or longer, although as the disease progresses there is a tendency for subsequent remissions to be shorter. The following case history shows a remission of three months following a remission of one month. A later remission of over fourteen months was induced by the use of Fowler's solution.

CASE V: Woman, age 43 years. Chronic myelogenous leukemia, with a previous duration of about five years. The leukocyte count at the beginning of therapy was 89,200 per cu. mm. Treatments, twelve in number, were given over an area 20 × 20 cm. on the abdomen in the course of five weeks, 25 r each time (total 300 r). The lowest point in the leukocyte curve after this treatment was 32,000 per cu. mm.; four weeks later the count had risen to 85,400, and in two more months to 144,000 per cu. mm., with a red blood cell count of 1,740,000. Although the prognosis seemed hopeless at this time, the patient was given three exposures alternating over the anterior and posterior surfaces of the spleen area, 30 r on three consecutive days (field 20 × 20 cm., total 90 r). There was a rapid fall in the number of leukocytes to 33,000 per cu. mm., and the remission lasted for four months. The leukocyte count then rose to 96,000. The count fell after the use of Fowler's solution and for the next fourteen months the leukocyte and red blood cell counts were normal, no treatment of any kind being used during this period. Subsequently there was a relapse associated with a high leukocyte count, great immaturity of the white cells, and hemorrhage into the brain, followed by death.

SUMMARY AND CONCLUSIONS

In the cases studied the diagnosis was usually made by the physician and it was left to the radiologist to plan and give the x-ray therapy. In many cases a hematological remission was not produced, or was obtained only after weeks of therapy. If a relapse followed soon after, it was often attributed to the vagaries of the disease. Yet it is known that many patients with fairly mature blood cells do respond well to proper therapy. It is our impression from the cases studied that it takes a longer time to produce a remission when the treatments are given on alternate days or at three-day or one-week intervals, and the remissions are shorter, than when the dose is given on successive days and discontinued when the leukocyte count falls to between 60,000 and 80,000 per cu. mm.

The factors of anemia, fever, and platelet number are not of primary significance in themselves as contraindications to x-ray therapy, but are useful in evaluating the underlying conditions. When a decrease in the number of red blood cells or platelets is an expression of the crowding of the marrow with fairly mature leukemic cells, roentgen therapy is indicated and is of value. When the anemia and thrombocytopenia reflect the crowding of the

marrow with blast cells, irradiation is definitely contraindicated. With the same number of r, the effects are more pronounced, the larger the field, and the results vary with the region exposed. Leukopenia after x-ray therapy is not necessarily permanently harmful. The status of the cells in the marrow, spleen, or lymph nodes is the underlying factor which determines whether or not the response is good, and this characteristic may or may not be evident from the peripheral blood. Age and sex in themselves are apparently only secondary factors in the prognosis. The basal metabolic rate, in so far as it indicates the degree of activity of the leukemic process is a guide to therapy, unless there is gross immaturity of the cells (predominantly myeloblasts, lymphoblasts, or monocyte blasts).

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The Experimental Production of Extraskeletal Bone-Forming Neoplasms in the Rat[1]

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BONE-CONTAINING neoplasms which have no connection with the skeleton are occasionally observed in man. Raso (1), in 1937, reported an osteoid chondrosarcoma of the breast and collected from the literature, dating from 1835, 74 mammary gland tumors containing bone or cartilage. Of the malignant tumors in this group, 27 were osteosarcomata, chondrosarcomata, or osteochondrosarcomata, 7 were primarily carcinomata, and 5 were mixed tumors. Binkley and Stewart (2) in 1940 discussed 9 cases of tumors of epithelial origin resembling osteogenic sarcomata and concluded that the most important alterations leading to the appearance of the structure of osteogenic sarcoma are the laying down of dense hyaline tissue and the development of a cavernous telangiectatic type of circulation favoring stasis. They recognized that these features fail to explain the structure of cartilage in these so-called mixed tumors. Allen (3), 1940, described 4 mixed tumors of the mammary glands of dogs and one from the human breast. He concluded that in 3 of the canine neoplasms the cartilage was derived directly from adult epithelium. The strikingly high incidence of bone and cartilage in breast tumors of dogs he ascribed to liability to trauma and the rectiform pattern of the canine acinar epithelium. Wilson (4), 1941, collected from the literature 30 cases of malignant bone-forming tumors of the soft tissues with histologic pictures of true osteogenic sarcomata and added 10 new cases as illustrations of the totipotency of neoplastic mesoblastic tissue. The literature contains numerous additional descriptions of bony and cartilaginous neoplasms of the thyroid, uterus, ovary, lung, pleura, kidney, bladder, fascia, and meninges.

The first experimentally produced osteosarcoma was reported by Russell (5) in 1923. He described an osteosarcoma of the subcutaneous tissues of a rat at the site of repeated tar injections. The neoplasm was observed six months after the cessation of injections and was a polymorphous-cell sarcoma with bony particles scattered throughout the growth. It was readily transplantable, but osteoid tissue was found in only two growths of the first generation of transplantation. In these two instances the tumors had grown slowly, persisting for ninety-three and ninety-eight days, respectively. Russell concluded that the metaplasia required a long period to unfold itself and that its absence in subsequent generations could be attributed to the rapid growth of the soft tissue, which generally destroyed the rats long before three months had elapsed.

CYSTICERCUS-INDUCED NEOPLASMS

In 1925, Bullock and Curtis (6) reported 4 experimentally induced tumors in the rat's liver which contained hyaline cartilage. These tumors were observed in a series of 1,400 Cysticercus-induced neoplasms and included one osteoid chondroma (the only benign neoplasm in the series), a chondrosarcoma, a mixed-cell sarcoma containing islands of cartilage, and an osteochondrosarcoma. In the latter case osteoid tissue, bone, and cartilage were identified in the peritoneal metastases. A fifth Cysticercus-induced bone-

[1] This study was undertaken under the direction of Dr. F. C. Wood at the Department of Cancer Research Columbia University, to whom the authors gratefully acknowledge their indebtedness for interest and encouragement. The paper was read by title at the Twenty-ninth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1–2, 1943.

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forming tumor was made the subject of a separate report (7). This was the sixth bone-forming tumor in a series of 2,100 induced neoplasms and was unique in being composed in part of malignant bile-duct epithelium. The bulk of the tumor was osteochondrosarcoma of rather diversified structure, containing a large proportion of cartilage, osteoid tissue, and bone of the trabeculated type without lamellations. The intercellular substance was of several different kinds, embracing fibrillar, hyaline, osteoid, cartilaginous, and osseous material. Intermingled with the intercellular substance were tumor cells in different stages of differentiation and showing wide variation in size. Some parts of the growth consisted solely of large polymorphous cells and toward the periphery the sarcoma merged into carcinomatous tissue. The carcinoma was composed for the most part of rather small, deeply staining cuboidal cells which showed a tendency to arrange themselves into alveoli, small groups or strands occasionally forming the lining of small acini. The carcinoma replaced a part of the wall of a Cysticercus cyst and infiltrated the liver. The host showed generalized peritoneal metastases, but only the diaphragm was examined microscopically. This showed the structure of a polymorphous-cell sarcoma and contained islands of osteoid tissue and bone. The rat had, in addition, two other transformed cysts of approximately equal size. These had the structural characteristics of polymorphous-cell sarcomata and were probably of independent origin. The two types of tissue in the mixed tumor were thought to represent independent processes, since there was no evidence to indicate that the sarcoma resulted from a malignant transformation of the stroma of the carcinoma.

In subsequent studies, bringing the number of Cysticercus-induced neoplasms observed in the rat's liver up to nearly 7,500, there were identified 43 additional bone-forming tumors. In this entire series, therefore, 49 or somewhat less than 1 per cent of the liver tumors contained bone,

TABLE I: MEAN LATENT PERIOD AND STANDARD DEVIATION OF A GROUP OF CYSTICERCUS-INDUCED NEOPLASMS AND THE NUMBER AND AVERAGE LATENT PERIOD OF THE BONE-FORMING TUMORS WITH THE SAME NUMBER OF CYSTS

No. of Cysts	Days/30 Mean	Days/30 S. D.	Number of Bone Tumors	Average Latent Period Days/30
1	18.8	3.8	6	18.9
4	17.4	3.4	8	15.6
7	16.6	3.2	8	17.2
10	16.5	2.5	1	16.3
13	15.5	2.3	6	16.6
16	14.5	2.4	4	17.9
19	13.9	2.4	2	12.0
22	14.5	1.9	5	14.8
25	14.6	2.3	2	17.3
28	13.7	2.2	3	14.2
30–34	13.3	1.8	1	11.9
35–39	13.5	1.9	1	9.0
40–44	13.6	1.7	.	..
45–49	12.8	1.6	.	..
50–54	12.9	1.7	1	12.6
55–59	12.7	1.5	.	..
60–64	12.2	1.9	1	12.3

cartilage, or osteoid tissue; 21 resembled true osteogenic sarcomata; 26 were primarily fibrosarcomata containing islands of osteoid tissue, bone, or cartilage; 2 were benign chondromata. These observations are of especial interest in view of the results obtained by Huggins (8) in a series of well controlled experiments on heteroplastic bone formation in dogs following the transplantation of bladder epithelium. Huggins found that transplants of epithelium from the urinary bladder separated from their own fascia invariably initiated bone formation in the rectus muscle, subcutaneous tissues, fascia lata, and synovial cavity of the knee joint, while in the parenchyma of the kidney, liver, or spleen the regenerating epithelium formed cysts surrounded by similar appearing connective tissue but no bone. These experiments demonstrated the nonspecificity of osteoblasts, since other connective tissue under an altered environment acquired osteogenic properties, but Huggins concluded, further, that there are two types of fibrocytes: those which ossify, such as the connective tissues of the fatty-fibrous subcutaneous tissue, striated muscle, and fasciae, and those without the capacity to ossify, from the kidney, liver, and spleen.

Obviously the fibroblasts of the liver

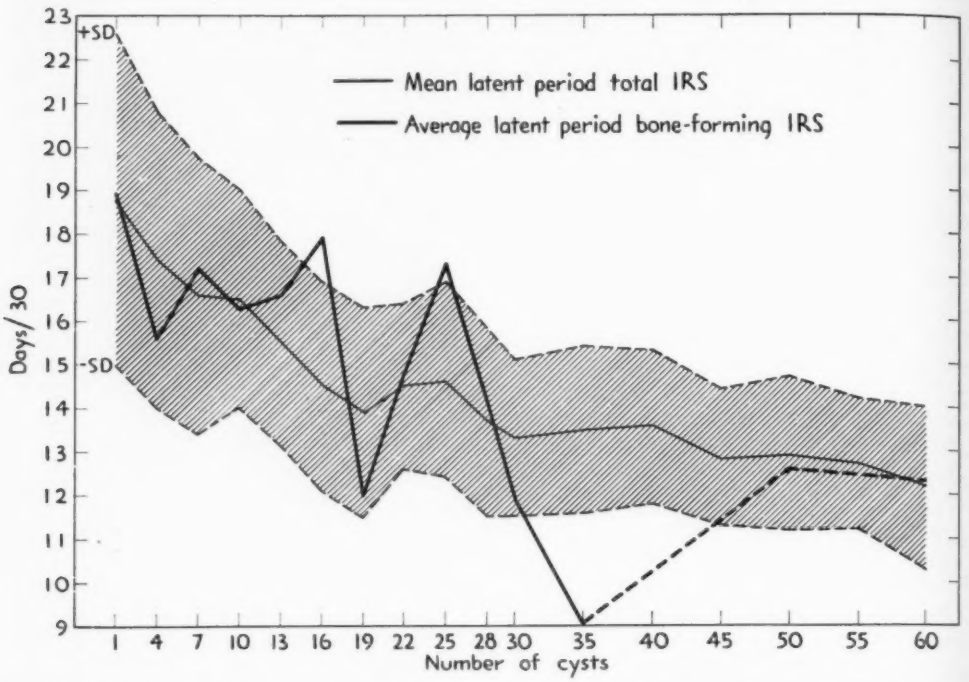

Chart 1. The mean ± S. D. latent period of Cysticercus-induced neoplasms and the average latent period of Cysticercus-induced bone-forming tumors.

of the rat may assume osteogenic properties under some as yet obscure conditions. Inspection of the available data on the 49 neoplasms mentioned above failed to reveal any contributing factor. These rare neoplasms were observed in rats infested with from 1 to as many as 64 Taenia larvae and were distributed among each of the several lobes of the liver as follows: right median 19, right lateral 9, left median 7, left lateral 7, caudate 4, hilus 1; in 2 instances the exact location was undetermined. The hosts were of 5 different inbred strains, represented as follows: A × C, 17; Fischer, 10; Copenhagen, 7; August, 6; Zimmerman, 2; hybrids 7, approximating the proportional distribution of the tumor-bearing rats of the colony, which practically eliminates the possibility of an hereditary constitutional factor. Thirty-six of the tumors were observed in male and only 13 in female rats, but in a population (9) in which the males were previously shown to have 17 per cent more parasitic cysts than the females this difference is probably not significant.

The average latent period is dependent upon the number of parasitic cysts and, as shown in Table I and Chart 1, when the latent periods for the tumors of this small group are compared with the mean latent periods previously observed (10) for nearly 4,000 Cysticercus-induced sarcomata, it appears that this group shows more than the expected range of variation for tumor bearers with the same number of cysts. In 3 instances the average fell outside the area bounded by the mean ± the standard deviation. In 8 of the 14 classes the average latent period of the bone-forming tumors was longer than that observed for the large group. In spite of the evidence which follows, however, it cannot be convincingly argued that the process of osteogenesis requires a longer time or that an exceptional parasite elaborating less incitant was a determining factor, since in a few instances these bone-forming tumors

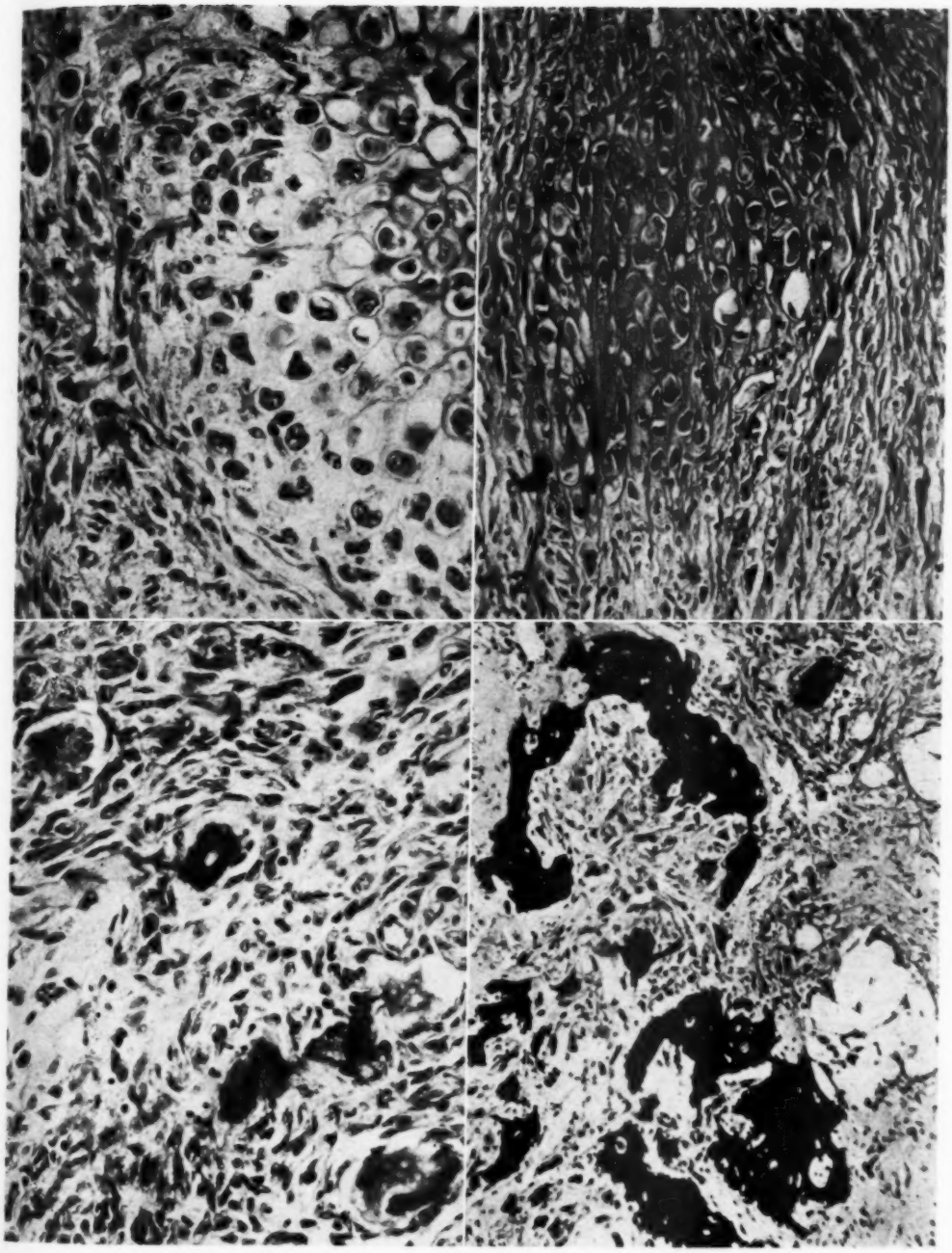

Fig. 1. Chondrosarcoma of rat (Tumor B-P 1163) ×260.
Fig. 2. Fibrosarcoma with islands of osteoid tissue (Tumor B-P 1696) ×260.
Fig. 3. Fibrosarcoma with areas of bone formation (Tumor B-P 1813) ×260.
Fig. 4. Fibrosarcoma with areas of calcification (Tumor B-P 2159) ×150.

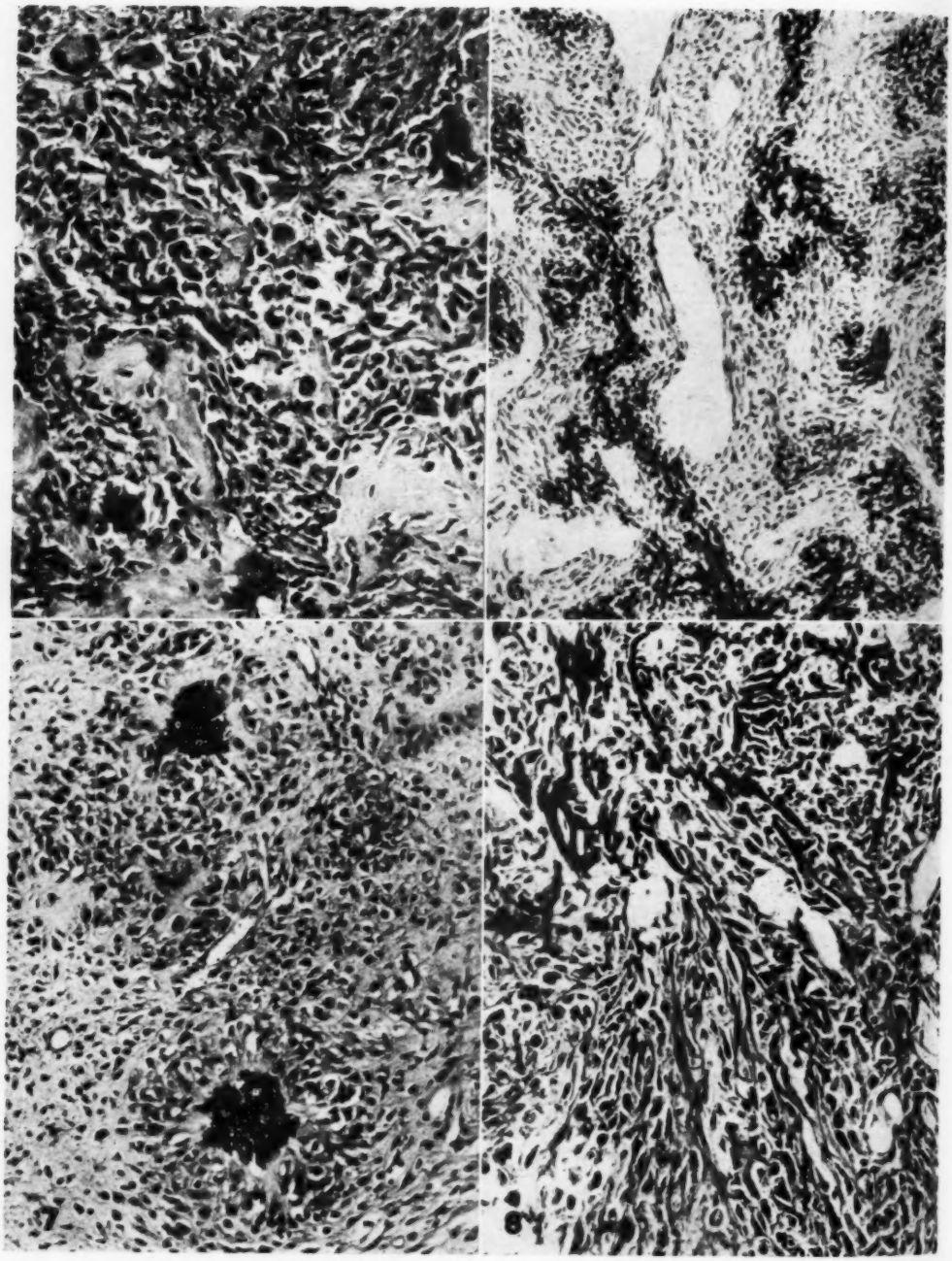

Fig. 5. Osteosarcoma (Tumor B-P 2115) ×260.
Fig. 6. Osteosarcoma (Tumor B-P 1847) ×137.5.
Fig. 7. Osteosarcoma (Tumor B-P 2243) ×137.5.
Fig. 8. Osteosarcoma (Tumor B-P 2294) ×260.

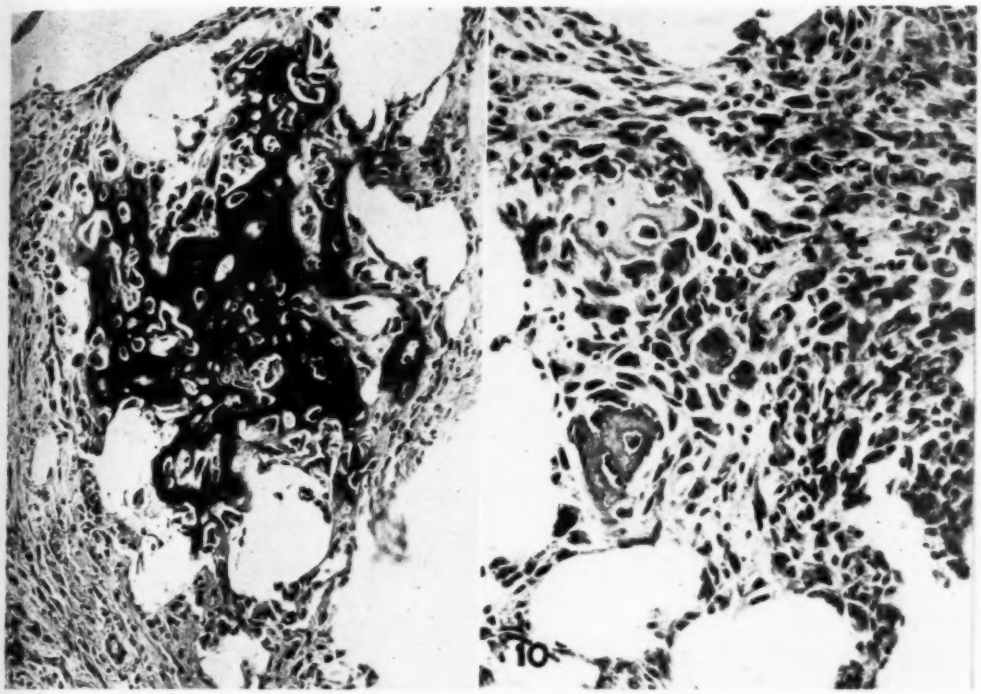

Fig. 9. Early osteosarcoma (Tumor B-P 2717) ×137.5.
Fig. 10. Early osteosarcoma (Tumor B-P 2770) ×260.

developed in a shorter period than was observed as the mean for a much larger group of induced sarcomata which did not produce bone.

Contrary to observations on human osteogenic sarcomata, these hepatic bone-forming tumors were no more malignant than the non-bone-forming neoplasms of the same series. Thirty-six of the 49 tumor hosts showed a generalized peritoneal dissemination of the tumor, and in only 11 was bone or cartilage demonstrable in the metastases examined. Thirteen or 27 per cent had no gross metastases. In a previously reported series (11) of 3,677 Cysticercus-induced tumors, 27 per cent were found to have no demonstrable metastases. In a study of human osteogenic sarcomata, MacDonald and Budd (12) found osteosarcomata more malignant than chondrosarcomata, and fibrosarcomata distinctly less malignant. In this group of liver tumors, 26 were primarily fibrosarcomata, 10 chondrosarcomata, and 11 osteosarcomata. Twenty, or approximately 80 per cent of the first group, had peritoneal metastases, and in 7 of these bone was demonstrable. Eight of each of the other two classes had generalized secondary growths; cartilage was present in the metastases of 3 of the bearers of chondrosarcomata and bone was found in the peritoneal metastases of only one of the bearers of osteosarcomata. That is, the differences in morphology were not reflected in the relative malignancy of these neoplasms.

BENZPYRENE-INDUCED NEOPLASMS

In a series of 2,351 neoplasms induced in rats by the subcutaneous injection of paraffin containing 3:4-benzpyrene, 66 or nearly 3 per cent were osteosarcomata, chondrosarcomata, or fibrosarcomata containing areas of cartilage, osteoid tissue, or bone. Two of these osteoid sarcomata

TABLE II. CLASSIFICATION OF THE TUMORS INDUCED BY 1 PER CENT BENZPYRENE IN EACH STRAIN OF RATS AND THE PERCENTAGE IN MALES AND FEMALES

Classification	Strain							Total	Per Cent	
	August	Fischer	Marshall	A × C	Sherman	Misc.	Hybrid		Male	Female
Spindle-cell sarcoma and fibrosarcoma	145	79	282	469	154	51	320	1,500	75.46	78.55
Rhabdomyosarcoma	5	2	...	2	9	..	4	22	0.65	1.72
Sarcoma, myogenic?	33	21	35	87	82	5	68	331	19.44	13.88
Fibroma	...	1	3	2	...	..	...	6	0.46	0.11
Liposarcoma	3	...	2	8	1	2	2	18	0.83	1.03
Bone-forming sarcoma	...	1	7	8	1	..	7	24	1.30	1.14
Adenocarcinoma	1	...	...	2	...	..	...	3	0.09	0.23
Squamous-cell carcinoma	...	1	...	7	1	..	6	15	0	1.72
Adenocarcinoma and sarcoma	1	...	...	2	...	..	...	3	0	0.34
Squamous-cell carcinoma and sarcoma	...	...	1	...	...	..	...	1	0.09	0
Endothelioma	1	...	1	4	...	..	...	6	0.28	0.34
Myxosarcoma	4	3	4	4	...	..	2	17	1.11	0.57
Neurosarcoma	1	...	...	...	...	..	...	1	0.09	...
Adenoma	...	...	1	...	...	..	2	3	0.09	0.23
Lipoma	...	...	...	1	1	..	...	2	0.09	0.11
Sum	194	108	336	596	249	58	411	1,952	1,080	872
Early sarcoma	9	12	27	76	17	1	58	200	103	97
Unclassified	5	6	30	38	6	3	13	101	51	50
TOTAL	208	126	393	710	272	62	482	2,253	1,234	1,019

TABLE III: CLASSIFICATION OF THE TUMORS INDUCED BY 0.25 PER CENT BENZPYRENE IN EACH STRAIN OF RATS AND THE PERCENTAGE IN MALES AND FEMALES

Classification	Strain							Total	Per Cent	
	August	Fischer	Marshall	A × C	Sherman	Misc.	Hybrid		Male	Female
Spindle-cell sarcoma and fibrosarcoma	16	37	29	39	65	17	56	259	87.82	82.74
Rhabdomyosarcoma	..	1	..	..	1	..	..	2	0.61	0.72
Sarcoma, myogenic?	1	4	2	1	..	1	1	10	4.88	1.44
Liposarcoma	..	..	..	1	..	..	..	1	0.61	...
Bone-forming sarcoma	2	1	3	2	3	..	10	21	548	8.63
Adenocarcinoma	..	..	1	..	..	..	..	1	0	0.72
Endothelioma	..	1	..	..	..	..	..	1	0	0.72
Myxosarcoma	..	..	..	..	1	..	1	2	0	1.44
Adenoma	..	1	..	..	4	..	1	6	0.61	3.60
Sum	19	45	35	43	74	18	69	303	164	139
Early sarcoma	1	11	6	8	4	2	5	37	18	19
Unclassified	2	2	6	8	8	3	1	30	10	20
TOTAL	22	58	47	59	86	23	75	370	192	178

have been previously reported (13). The morphology of the tumors varied considerably. Only 3 were chondrosarcomata (Fig. 1), and 28 were primarily fibrosarcomata with islands of osteoid tissue (Fig. 2), small areas of bone formation (Fig. 3), or extensive areas of calcification (Fig. 4). The largest group consisted of osteosarcomata, but these differed in relative quantity of bone and extent of calcification as illustrated in Figures 5–8. That the bone formed an integral part of the neoplasm from its initiation is well demonstrated in the tumors shown in Figures 9 and 10. Both were early sarcomata discovered by microscopic examination of the wax cysts.

These bone-forming neoplasms were observed in rats of both sexes of seven different inbred strains and were induced by

TABLE IV: CLASSIFICATION OF THE TUMORS INDUCED BY 0.10 PER CENT BENZPYRENE IN EACH STRAIN OF RATS AND THE PERCENTAGE IN MALES AND FEMALES

Classification	Strain						Total	Per Cent	
	Copen	Marshall	A × C	Sherman	Misc.	Hybrid		Male	Female
Spindle-cell sarcoma and fibrosarcoma	28	10	2	19	8	4	71	86.80	58.14
Fibroma	1	..	..	..	..	..	1	1.89	0
Bone-forming sarcoma	9	6	1	4	1	..	21	11.32	34.89
Adenocarcinoma	..	1	..	..	1	..	2	...	4.65
Adenoma	..	..	..	1	..	..	1	0	2.33
Sum	38	17	3	24	10	4	96	53	43
Early sarcoma	7	3	1	7	2	..	20	9	11
Unclassified	6	1	2	1	..	1	11	7	4
TOTAL	51	21	6	32	12	5	127	69	58

three concentrations of benzpyrene. Tables II, III, and IV give, respectively, the classification of the tumors induced by 1.0 per cent, 0.25 per cent, and 0.10 per cent benzpyrene. From Table II it appears that 24 or 1.2 per cent of the 1,952 classified neoplasms induced by 1.0 per cent benzpyrene were bone-forming sarcomata and that these peculiar tumors occurred with about equal frequency in males and females of this group. From Table III it appears that 21 or nearly 7 per cent of the 303 classified tumors induced by 0.25 per cent benzpyrene were bone-forming sarcomata. These bone-forming tumors represented about 5 per cent of the neoplasms induced in males and nearly 9 per cent of the tumors induced in females by this concentration of benzpyrene. Further, Table IV shows that among 96 classified tumors induced by 0.1 per cent benzpyrene, 21 or more than 20 per cent were bone-forming sarcomata. These osteosarcomata represented 11 per cent of tumors induced in males and nearly 35 per cent of those induced in females by this concentration of the incitant. The several inbred strains were not equally represented in the three groups, but bone-forming sarcomata were observed with about equal frequency in each of 7 inbred strains and in the hybrids, thus reducing the possibility of an inherited constitutional predisposing factor. The sex differences were more apparent in the smaller groups and are probably biologically insignificant, since they are in the opposite direction of the difference observed among the Cysticercus-induced bone-forming sarcomata in the liver.

That the concentration of the incitant was a factor in determining the morphology of these neoplasms is readily seen by a comparison of Tables II, III, and IV. The reduction in the concentration of the benzpyrene significantly increased the proportion of induced bone-forming sarcomata, while it otherwise limited variation in the histogenesis of the induced neoplasms. Although the two series induced by 0.25 per cent and 0.10 per cent benzpyrene were smaller than the series induced by 1 per cent benzpyrene, the absence in the former of any neoplasms containing squamous epithelium is probably significant. It is interesting, further, to compare the morphology of these benzpyrene-induced tumors with a previously reported (14) series of neoplasms induced in the same manner with 1.0 and 0.5 per cent methylcholanthrene. Among approximately 800 tumors induced by methylcholanthrene, no bone-forming neoplasms were identified, but there were 11 tumors composed, in part at least, of malignant squamous epithelium. Evidently, the somewhat more rapidly effective carcinogen and the more concentrated benzpyrene, which was able to penetrate the fibrous capsule of the wax cyst and initiate local squamous metaplasia of the cells lining the mammary ducts that occasionally terminated in squamous-cell cancer, were less effective in inducing

TABLE V: FOR TUMORS INDUCED WITH 1 PER CENT BENZPYRENE, THE MEAN NUMBER OF DAYS TO OBSERVATION AND DEATH, THE MEAN DIAMETER AT AUTOPSY, AND THE MEAN DAILY INCREASE IN DIAMETER IN MILLIMETERS

Group	No. of Tumors	Mean Days to Observation	Mean Days Observation to Death	Mean Diameter in mm.	Mean Daily Increase in Diameter in mm.
2 mg.	103	194 ± 6	36 ± 1.4	33.3 ± 0.8	0.70 ± 0.04
4 mg.	2 9	164 ± 2	32 ± 1.1	30.9 ± 0.7	0.66 ± 0.02
6 mg.	283	151 ± 2	36 ± 1.1	30.0 ± 0.6	0.66 ± 0.02
8 mg.	176	143 ± 2	26 ± 0.9	29.0 ± 0.8	0.67 ± 0.03
10 mg.	153	148 ± 2	24 ± 1.2	26.4 ± 0.8	0.63 ± 0.03
12 mg.	194	148 ± 2	21 ± 0.8	25.7 ± 0.6	0.67 ± 0.03
16 mg.	49	117 ± 2	23 ± 1.7	26.1 ± 1.3	0.69 ± 0.05
24 mg.	77	118 ± 2	18 ± 1.1	22.0 ± 0.7	0.77 ± 0.05
Total with 1 tumor	219	177 ± 4	35 ± 1.0	34.1 ± 0.6	0.70 ± 0.03
Total first tumors	369	136 ± 2	35 ± 0.7	34.5 ± 0.5	0.70 ± 0.02
Subsequent tumors	676	152 ± 1	21 ± 0.6	22.5 ± 0.3	0.62 ± 0.02
SUM	1,264	152 ± 1	27 ± 0.5	28.7 ± 0.3	0.69 ± 0.01

TABLE VI: FOR TUMORS INDUCED WITH 0.25 PER CENT BENZPYRENE, THE MEAN NUMBER OF DAYS TO OBSERVATION AND DEATH, THE MEAN DIAMETER AT AUTOPSY, AND THE MEAN DAILY INCREASE IN DIAMETER IN MILLIMETERS

Group	No. of Tumors	Mean Days to Observation	Mean Days Observation to Death	Mean Diameter in mm.	Mean Daily Increase in Diameter in mm.
0.5 mg.	24	267 ± 13	54 ± 7.0	35.1 ± 2.0	0.57 ± 0.05
1.0 mg.	44	245 ± 11	42 ± 3.1	30.4 ± 1.8	0.48 ± 0.05
1.5 mg.	71	268 ± 9	45 ± 2.6	34.6 ± 1.4	0.58 ± 0.04
2.0 mg.	74	251 ± 7	46 ± 2.7	32.9 ± 1.5	0.55 ± 0.04
2.5 mg.	59	242 ± 9	48 ± 3.6	31.6 ± 1.5	0.45 ± 0.04
3.0 mg.	98	271 ± 7	40 ± 2.2	28.3 ± 1.2	0.51 ± 0.03
Total with 1 tumor	125	228 ± 7	44 ± 2.3	35.7 ± 3.3	0.57 ± 0.03
Total first tumors	100	248 ± 6	53 ± 1.8	34.5 ± 1.8	0.51 ± 0.03
Subsequent tumors	145	293 ± 5	33 ± 2.1	20.7 ± 1.2	0.47 ± 0.04
SUM	370	259 ± 4	45 ± 1.3	28.3 ± 1.2	0.52 ± 0.02

TABLE VII: FOR TUMORS INDUCED BY 0.1 PER CENT BENZPYRENE, THE MEAN NUMBER OF DAYS TO OBSERVATION AND DEATH, THE MEAN DIAMETER AT AUTOPSY, AND THE MEAN DAILY INCREASE IN DIAMETER IN MILLIMETERS

Group	No. of Tumors	Mean Days to Observation	Mean Days Observation to Death	Mean Diameter in mm.	Mean Daily Increase in Diameter in mm.
0.2 mg.	7	294 ± 34	29 ± 7.8	29.5 ± 4.4	0.41 ± 0.11
0.4 mg.	13	301 ± 29	62 ± 14.0	27.5 ± 2.5	0.59 ± 0.14
0.6 mg.	24	344 ± 14	34 ± 3.1	30.4 ± 2.2	0.42 ± 0.07
0.8 mg.	26	285 ± 15	40 ± 4.1	35.0 ± 2.5	0.49 ± 0.08
1.0 mg.	24	290 ± 15	50 ± 5.1	34.5 ± 2.6	0.58 ± 0.06
1.2 mg.	33	323 ± 15	43 ± 6.1	27.5 ± 2.4	0.43 ± 0.07
Total with 1 tumor	48	301 ± 14	43 ± 4.0	30.9 ± 1.8	0.51 ± 0.05
Total first tumors	32	295 ± 13	47 ± 4.0	33.4 ± 1.6	0.45 ± 0.05
Subsequent tumors	47	342 ± 10	30 ± 5.0	28.5 ± 3.2	0.50 ± 0.10
SUM	127	315 ± 7	45 ± 3.0	31.6 ± 1.1	0.48 ± 0.03

bone-forming sarcomata than the dilute benzpyrene.

Further, it appears from Tables V, VI, and VII that the concentration of the localized incitant affected the rate of growth or malignancy of the induced neoplasms. Tumors induced by 1.0 per cent benzypyrene had an average increase in diameter of 0.69 ± 0.01 mm. per day, while the average daily increase in diameter of the tumors induced by 0.25 per cent and 0.10 per cent benzpyrene was, respectively, 0.52 ± 0.02 and 0.48 ± 0.03 mm. At autopsy the tumors in the three groups were

of nearly equal average diameter, *i.e.*, 30 mm. The rats with tumors induced by 1.0 per cent benzpyrene lived an average of about thirty days after the tumors were observed, while the bearers of tumors induced by the more dilute benzpyrene lived an average of forty-five days. There appear to be no significant differences which can be attributed to the total dose or number of foci of irritation in the host or to whether the induced neoplasm was the first of multiple tumors, a subsequently observed neoplasm, or the only tumor induced in the host. For each dose and each class of tumor the average rate of growth was consistently higher for the neoplasms induced by the strongest concentration of benzpyrene.

When the bone-forming neoplasms were similarly tabulated, as shown in Table VIII, it appears that the 24 which were induced by the 1.0 per cent benzpyrene had a longer average latent period, longer average period from observation to autopsy, and a smaller average daily increase in diameter than the average of the non-bone-forming neoplasms of the series. That is, the bone-forming tumors in this

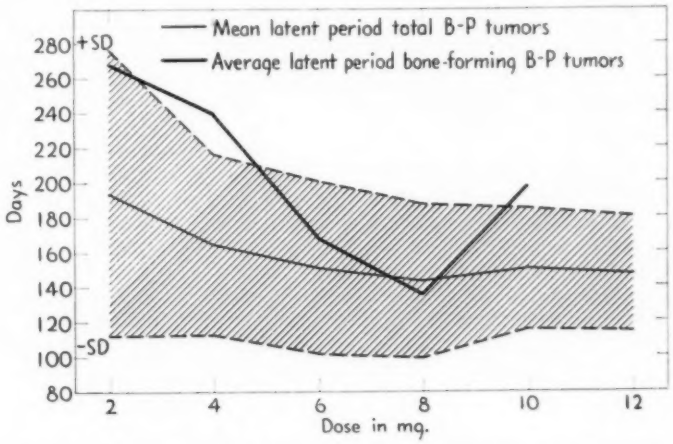

Chart 2. The mean ± S. D. latent period for tumors induced by 1 per cent benzpyrene and the average latent period of the bone-forming sarcomata.

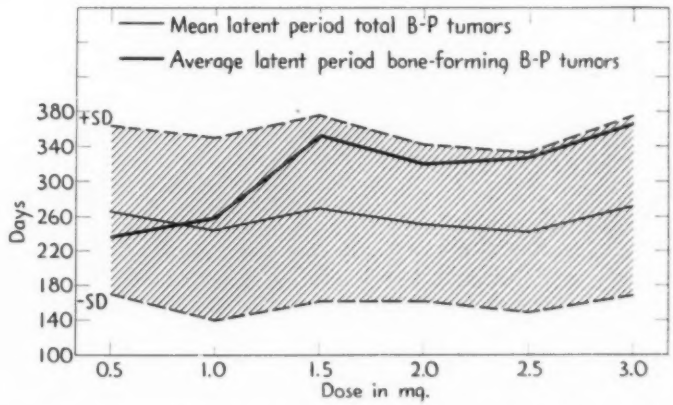

Chart 3. The mean ± S. D. latent period of tumors induced by 0.25 per cent benzpyrene and the average latent period of the bone-forming sarcomata.

TABLE VIII: FOR THE BONE-FORMING NEOPLASMS, THE AVERAGE DAYS TO OBSERVATION AND DEATH, THE AVERAGE DIAMETER AT AUTOPSY, AND THE AVERAGE DAILY INCREASE IN DIAMETER IN MILLIMETERS

Group	No. of Tumors	Average Days to Observation	Average Days Observation to Death	Average Diameter in mm.	Average Daily Increase in Diameter in mm.
1 per cent					
2.0 mg.	9	268	46	36	0.49
4.0 mg.	5	239	24	36	0.55
6.0 mg.	8	168	50	32	0.31
8.0 mg.	1	136	34	16	0.20
10.0 mg.	1	197	7	16	0.40
SUM	24	220	41	32	0.41
0.25 per cent					
0.5 mg.	1	238	23	24	0.64
1.0 mg.	3	257	32	..	..
1.5 mg.	5	355	42	35	0.66
2.0 mg.	5	319	75	36	0.38
2.5 mg.	4	325	57	34	0.47
3.0 mg.	3	367	79	22	0.11
SUM	21	323	64	32	0.53
0.10 per cent					
0.4 mg.	1	304	..	..	..
0.6 mg.	9	384	24	17	0.39
0.8 mg.	3	340	84	30	0.43
1.0 mg.	3	223	56	25	0.68
1.2 mg.	5	293	37	14	..
SUM	21	329	52	22	0.46

series were more characteristic of the tumors induced by the weaker concentrations of benzpyrene. Charts 2 and 3 compare the average latent periods of the bone-forming tumors induced by 1.0 per cent and 0.25 per cent benzpyrene, respectively, with the mean latent period ± the standard deviation of the total tumors induced by the same concentrations of benzpyrene. Except for one tumor induced in a rat receiving 8 mg. of benzpyrene and one induced by 0.5 mg. of benzpyrene, the average latent period of the bone-forming neoplasms of both series exceeded the mean observed for the series as a whole. Since the average latent period is determined by the dose of the carcinogen and the bone-forming tumors occurred most characteristically with dilute concentrations of benzpyrene, it may be postulated that the few which were observed with the higher concentration of benzpyrene may have resulted from individual foci in some manner depleted of the active agent.

Table IX shows the classification and rate of growth of the bone-forming neoplasms induced by each of the three concentrations of benzpyrene. The tumors are arranged in the order of malignancy reported by MacDonald and Budd (12) for human osteogenic sarcoma. Since the tumors induced by 1.0 per cent benzpyrene tended to be more malignant as a group than those induced by the weaker concentrations of the incitant, it is surprising to find that the proportion of osteosarcomata was higher among the tumors induced by the two weaker concentrations of benzpyrene, and chondrosarcomata, which MacDonald and Budd found to be intermediate in malignancy, occurred only among the tumors induced by the highest concentration of benzpyrene. However, the bone-forming tumors which were primarily fibrosarcoma tended to be less malignant than the osteosarcomata. The average daily increases in diameter of the former were 0.39, 0.34, and 0.28 mm., while for the osteosarcomata induced by the three concentrations of benzpyrene the corresponding figures were 0.50, 0.64, and 0.57 mm. Even though these averages were based on a very few cases of induced heteroplastic bone-forming neoplasms in the rat, they agree with the observations of MacDonald and Budd on the rate of growth of human osteogenic sarcomata.

TABLE IX: NUMBER OF BONE-FORMING TUMORS OF EACH CLASS, THE NUMBER (IN PARENTHESES) WHICH WERE CHARTED, AND THE AVERAGE DAILY INCREASE IN DIAMETER IN MILLIMETERS OF THE CHARTED TUMORS

Classification	1 Per Cent		0.25 Per Cent		0.10 Per Cent	
	No. of Tumors	Ave. Daily Increase in Diameter in mm.	No of Tumors	Ave. Daily Increase in Diameter in mm.	No. of Tumors	Ave. Daily Increase in Diameter in mm.
Fibrosarcoma	15 (11)	0.39	5 (4)	0.34	8 (2)	0.28
Chondrosarcoma	3 (3)	0.33	0	..	0	..
Osteosarcoma	6 (4)	0.50	16 (7)	0.64	13 (3)	0.57
Total	24 (18)	0.41	21 (11)	0.53	21 (5)	0.46

SUMMARY

1. Among 7,500 neoplasms induced in the rat's liver by *Cysticercus fasciolaris*, 49 were bone-forming tumors. Six of these have been previously reported.

2. These rare bone-forming tumors were fortuitously distributed in the several lobes of the liver, in five different inbred strains of rats, and varied, like the non-bone-forming neoplasms of the series, from benign to highly malignant growths. The hosts had from 1 to 64 parasitic cysts and the latent period was extremely variable.

3. Sixty-six bone-forming neoplasms were observed in a series of 2,351 tumors induced in rats by the subcutaneous injection of paraffin containing 3:4-benzpyrene. These neoplasms occurred in rats of both sexes of seven different inbred strains.

4. The bone-forming neoplasms were induced by three concentrations of benzpyrene, namely, 1.0 per cent, 0.25 per cent, and 0.10 per cent, and comprised 1.0 per cent, 7.0 per cent, and 20.0 per cent of the tumors induced by these respective concentrations of the incitant.

5. The concentration of the incitant affected the rate of growth and malignancy of the induced neoplasms. Tumors induced by 1.0 per cent benzpyrene had a shorter latent period, a greater average daily increase in diameter, and killed the host in a shorter average interval after observation than the tumors which were induced by weaker concentrations of benzpyrene.

6. The bone-forming neoplasms induced by 1.0 per cent benzpyrene had a longer average latent period, longer average period from observation to death, and a smaller average daily increase in diameter than the average of the series. In these characters, they resembled the tumors induced by the weaker concentrations of benzpyrene.

7. The most favorable incitant of heteroplastic bone-forming neoplasms was 0.10 per cent benzpyrene in paraffin, the weakest concentration of incitant thus far tested.

8. The osteosarcomata had a greater average daily increase in diameter than the bone-containing neoplasms, which were primarily fibrosarcomata.

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CASE REPORTS

So-Called "Subperiosteal Giant-Cell Tumor"[1]

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Very few so-called subperiosteal giant-cell tumors have been reported, and an interesting diagnostic problem is offered when one is seen radiographically. Geschickter and Copeland (1) reported but four such cases in their series and noted that all had been published since January 1926. They point out the characteristic history of trauma and the short duration of symptoms. These features were noted, also, in the cases of Cone (2) and Potts (3).

The striking microscopic observation of multinucleated giant cells and the osteogenic response of the periosteum has given the name of subperiosteal giant-cell tumor to this condition, which histologically bears a close resemblance to giant-cell tumor of bone. It is believed by MacCallum (4), Cone (2), and Geschickter and Copeland (1), to be a reparative process, a process modified by the cells and the mechanical factors present beneath the periosteum.

Radiographically a more or less completely encapsulated mass is seen, elevating the periosteum and excavating the adjacent cortical bone. No bone proliferation is apparent and there is no true medullary involvement. The latter condition may be suggested, however, by decreased density over the areas of eroded cortical bone.

A 33-year-old soldier was admitted to the Hoff General Hospital on Aug. 31, 1943, complaining of pain in the left forearm of two months' duration. Discomfort had been noticed a few hours after scuffling in company football, and there had been early mild swelling just below the elbow posteriorly. These symptoms were aggravated by use and at first varied in intensity. Subsequently, the pain became sharp and more persistent, and the swelling increased slowly. On Aug. 28 the patient presented himself for treatment at his station hospital, whence he was transferred to Hoff General Hospital with a diagnosis of "osteogenic sarcoma."

Physical examination on admission revealed a firm, circumscribed fusiform swelling on the dorsal aspect of the left radius at the junction of its proximal and middle thirds. Complete function was present except that supination was limited somewhat by pain. Tenderness was elicited on palpation.

Fig. 1. Subperiosteal giant-cell tumor of radius.

Roentgenograms revealed a well circumscribed, faintly calcified mass 5 cm. distal to the articular surface of the radial head (Fig. 1). It extended for 5 cm. along the shaft of the radius and was 2 cm. in width. Beneath it the cortical bone showed a saucer-like excavation, and the medullary bone contained several areas of apparent diminished density. The margins of the elevated periosteum or tumor were rounded and lacked the "triangle" so frequently seen in malignant neoplasms. The findings were interpreted as follows: "A benign tumor with subperiosteal hematoma as the most probable diagnosis. A malignant tumor cannot be entirely excluded."

Under an upper arm tourniquet the area of the mass on the dorsum of the left forearm was opened on Sept. 8, 1943, by Major Robert F. Warren, M.C. The tumor was found to be bluish-gray, about 5 cm. long and 4 cm. wide, and enclosed by an edematous capsule. Aspiration of 3 c.c. of bloody fluid by

[1] Accepted for publication in June 1944.

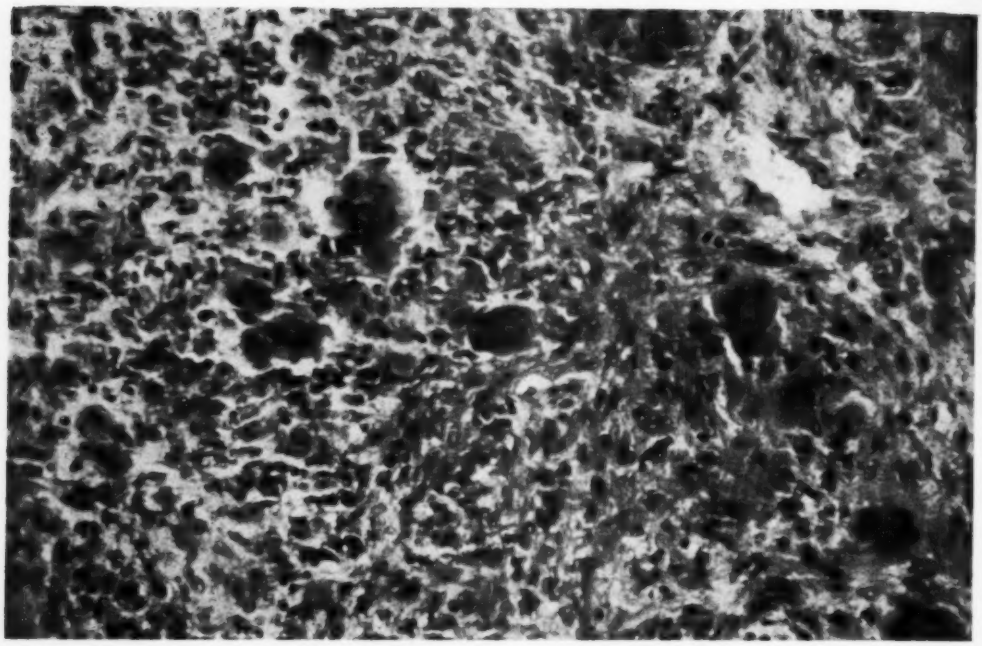

Fig. 2. Subperiosteal giant-cell tumor: pathological section.

needle caused the mass to collapse. The wall was then opened and was seen to be about 3 mm. thick. Just beneath it were many minute (1 mm.) nodules of cellular tissue, several of which were removed. On examining the cortex, an area of erosion 1 cm. in length and 3 mm. wide was found, which was filled by a mass of red, fleshy material. This was removed for frozen section. Thereafter the entire area of elevated periosteum was excised and the cortical bone rongeured away about the fissure. The wound healed promptly and the patient was discharged to duty.

Captain Cecil F. Baisinger, M.C., studied the tissue specimens. They were red, moderately firm, and grossly suggested granulation tissue. Some fine calcification could be readily identified. On the frozen sections a fibrous appearing osteoid tissue was seen, in which there were many large multinucleated giant cells with centrally placed nuclei (Fig. 2). This finding was confirmed by the paraffin sections, which showed the stroma to be cellular, the cells being mostly large, vesicular, and pale-staining, with poorly defined cytoplasm. Other cells were present, which were smaller, more dense, and with distinct nucleoli. In this stroma were many typical multinucleated giant cells, most of which had over fifteen nuclei. In addition there were many macrophages loaded with yellowish-brown granular pigment, and some recent hemorrhage was present. Areas of osteoid tissue were found which were acidophilic and much less cellular. Sections of decalcified bone showed erosion, with osteoclasts in apposition to the outer surfaces. Definite new bone formation was apparent in some areas. Pathological diagnosis: "Subperiosteal giant-cell tumor of the radius."

The findings in this case are typical of those ascribed to subperiosteal giant-cell tumor. The radiographic impression of a subperiosteal hemorrhage is not surprising, since there was a completely encapsulated, lightly calcified tumor which appeared to displace the periosteum. The benign nature of the condition was suggested by the complete capsule and the absence of new bone formation. The patchy areas of diminished density in the medullary portion of the bone with the erosion of the cortex, however, made it impossible to feel secure in this conclusion. A biopsy, under such circumstances, seemed indicated.

CONCLUSION

A case of so-called "subperiosteal giant-cell tumor" of the radius is reported in detail.

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Klippel-Feil Malformation: Report of a Case in an Adult

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According to Dyke (2) the so-called Klippel-Feil malformation of the cervical region of the spine was first described by Willett and Walsham in 1880. Other writers (1, 5, 6) disagree, attributing the first description to Klippel and Feil in 1912. In 1919 Feil compiled all the reported cases and published them in the form of a thesis (3, 6).

Congenital anomalies of the cervical spine were once considered uncommon (1, 3, 4), but in recent years they have been repeatedly described and are probably even more frequent than the case reports would indicate. In 1932, only 30 cases of the Klippel-Feil syndrome had been reported, chiefly in the French literature; 3 cases had been reported in America and 1 in England (1). In 1934 Willard and Nicholson (6) were able to collect 60 cases from the literature. A number of additional reports have appeared since that time.

The anomaly is characterized clinically by an absence or shortening of the neck, lowering of the hair line on the back of the neck, and limitation of motion, especially lateral bending, of the neck. Flexion, extension, and rotary movements are usually normal (5). All or most of the bodies of the cervical vertebrae may be fused (1, 2, 4, 6). The number of the cervical vertebrae may be diminished, the spinous processes may be fused, and often there is an irregular formation of the lateral masses and bodies. The arches of the vertebrae may fail to unite posteriorly, resulting in a spina bifida occulta. Often there are associated malformations of the ribs, such as cervical ribs, crowding of the ribs, fusion of the ribs, as well as congenital anomalies in other parts of the body. Fusion of the scapula with the cervical vertebrae may occur (2). Willard and Nicholson (6) give the following specific additional variations, which have been noted in reported cases: fusion of the atlas to the occiput; fusion of the first three vertebral bodies with fusion of the spines of the third, fourth, and fifth cervical vertebrae; fusion of the first and second cervical vertebrae with the third intact and the fourth, fifth, and sixth fused; fusion of the third, fourth, fifth, and sixth cervical bodies and fusion of the sixth and seventh cervical and first and second dorsal spinous processes; reduction to four cervical vertebrae; all cervical vertebrae fused in one mass with four cervical ribs and reduction of the dorsal vertebrae to eight; a posterior spina bifida occulta which may extend from occiput to thorax; fusion of the six upper dorsal vertebrae; fusion of first and second right ribs and two ribs arising from fourth dorsal vertebrae on the left, fusion of the fifth lumbar vertebra and the sacrum; dorsal spina bifida occulta and sacral rachischisis; oblique bodies of the cervical and dorsal vertebrae with a hemivertebra and unfused lamina. From this enumeration the wide range of variation is obvious.

The etiology of the malformation is uncertain, but all writers agree that, whatever the changes may be, they take place within the uterus, early in fetal development. Trauma (3, 6), arrest in development (4), intrauterine inflammation (3), irregular segmentation of the spine occurring in the early weeks of fetal life, and morbid conditions interfering with normal development of the fetus (1) have been given as causes. In 1919 Feil expressed the belief that a high spina bifida is the original lesion and that pressure and trauma later in fetal life cause the fusion and malformation (6).

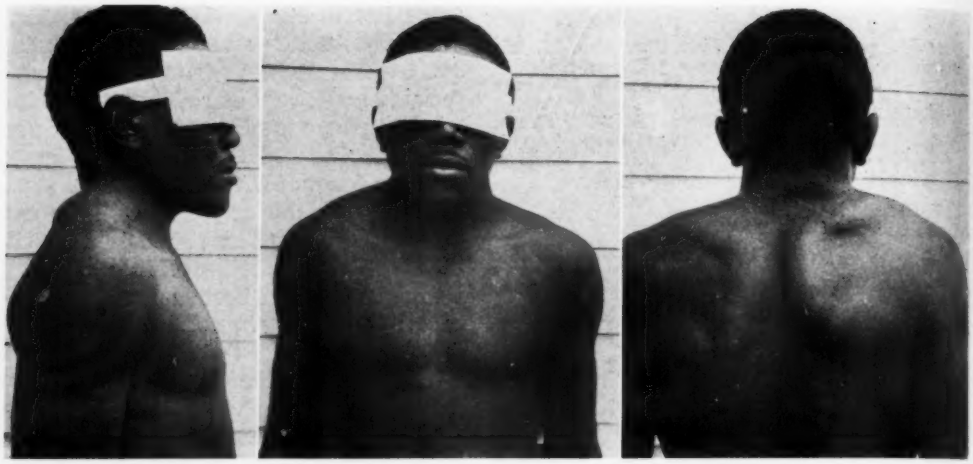

Fig. 1. Photographs of patient showing short neck and small lipoma in right scapular region, asymmetry of suprascapular regions due to elevation of right scapula, and low hair line.

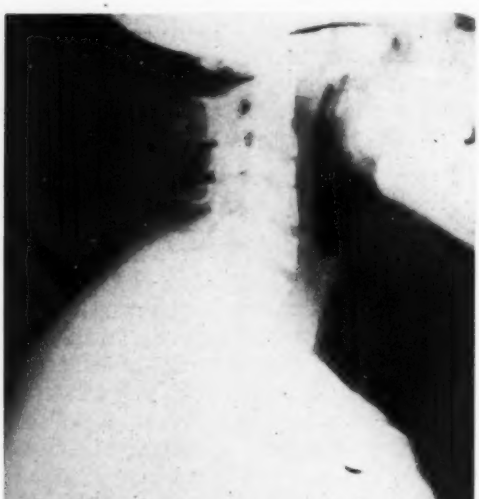

Fig. 2. Lateral roentgenogram of cervical spine showing deformities of bodies and spinous processes.

The lesion is most commonly confused with tuberculosis of the cervical spine, but can be differentiated from that disease by the absence of rigidity, motion without pain, and the roentgen findings. It may be associated with unilateral edema of the upper extremity, mirror movement or synkinesia, muscle spasm, constant contraction of the cervical muscles, high scapula (Sprengel's deformity), deformities of the shoulder and bones of the upper extremity, torticollis, facial asymmetry, dorsal scoliosis, difficulty in breathing or swallowing, shortness of breath, nystagmus, lesions of the brachial plexus, spastic paraplegia, sphincteric disturbances, neurotrophic joints, absence of the external auditory meatus, deafness, kyphosis, and mental deficiency.

There is no treatment for the deformity itself (1), although Willard and Nicholson (6) quote Heidecker as claiming improvement in mobility after gymnastic exercise. The condition, while most frequently found in children, is not incompatible with longevity, having been observed in a patient of seventy years (3).

CASE REPORT

A colored soldier, age 24, a native of North Carolina with seven months' Army service, was seen in the Orthopedic Out Patient Clinic of Station Hospital No. 1, Ft. Huachuca, Ariz., on June 23, 1943, complaining of a small tumor on his right shoulder, which caused him some difficulty in carrying his pack. He was sent to the X-Ray Department for an examination, which revealed elevation of the scapula and a malformation of the upper ribs and dorsal spine. The patient was admitted to the hospital for further study on June 30. His chief com-

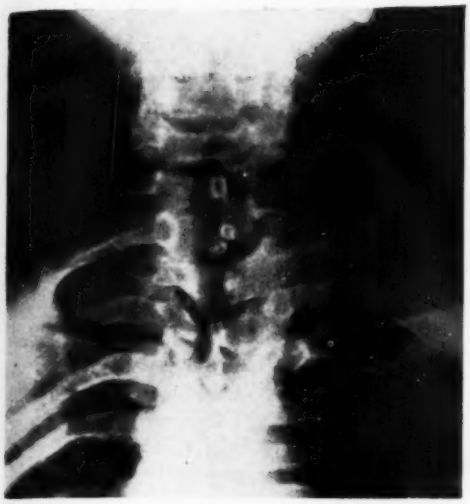

Fig. 3. Roentgenogram of thorax showing malformation of upper dorsal vertebrae and ribs.

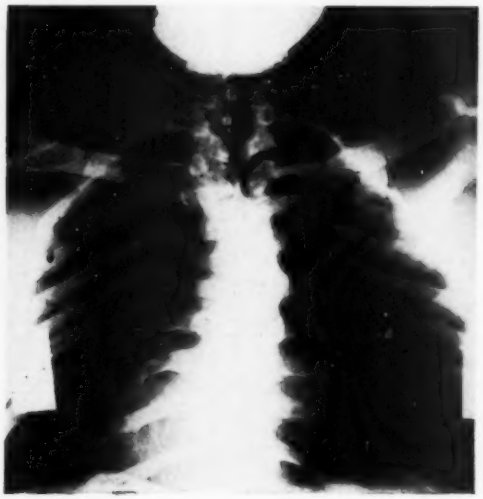

Fig. 4. Roentgenogram showing malformation of lower cervical and upper dorsal vertebrae and ribs.

plaint was still the small mass on his right shoulder. He gave a history of measles and malaria as a child and an injury to his right shoulder at the age of nine. He had had no tropical service, admitted the use of tobacco but denied the use of alcohol. There was no familial history of chronic or degenerative disease. His father, mother, four sisters, and four brothers were living and well. None showed any deformity.

The patient was intelligent and mentally alert and was anxious to get back to his company. His neck was thick and short and his hair line low. He could not move his neck laterally in either direction, but limited flexion, extension, and rotary motion were possible. There was a kyphosis of the upper dorsal spine. The right scapula was elevated, and there was a soft, freely movable soft-tissue mass, 6 cm. in diameter, just above the medial angle of the right scapula. No other evidence of disease, deformity, or congenital anomaly was noted. There was no evidence of synkinesia.

Roentgen examination of the thorax and spine revealed the following anomalies: (1) elevation of the right scapula; (2) fusion of the first cervical vertebra to the occiput; (3) fusion of the bodies of the second and third cervical vertebrae; (4) fusion of the spinous processes of the second and third cervical vertebrae; (5) narrowing of the body of the fourth cervical vertebra; (6) spina bifida occulta of the fourth cervical vertebra; (7) spina bifida occulta of the seventh cervical vertebra; (8) bifid spinous process of the fifth cervical vertebra; (9) partial fusion of the bodies of the seventh cervical and first dorsal vertebrae on the left side; (10) dorsal hemivertebrae; (11) deformed bodies of the upper dorsal vertebrae; (12) kyphosis of the upper dorsal spine; (13) right scoliosis of the dorsal spine; (14) right cervical rib; (15) fusion of the first and second ribs on the right at their vertebral articulation; (16) fenestration of the second rib on the right in the posterior axillary line; (17) a rudimentary right twelfth rib; (18) narrowing of the intercostal spaces in the left mid thorax; (19) thinning of the left fifth rib posteriorly.

SUMMARY

A case of malformation of the upper spine and thorax in a soldier who had engaged in strenuous infantry field training for seven months without symptoms is reported.

3036 Vine Grove Ave.,
St. Louis 15, Mo.

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EDITORIAL

Howard P. Doub, M.D., Editor

John D. Camp, M.D., Associate Editor

Lewis George Allen, M.D

In the choice of Lewis George Allen as President, the Radiological Society of North America has been fortunate. During the years of his membership Doctor Allen has demonstrated his willingness to assume responsibility and his ability to work diligently and with originality in the discharge of his duties. His was the task of formulating the plans and executing the details of the first Refresher Series presented by the Radiological Society, an undertaking which those who have had the opportunity of working with him know to have been an exacting one.

Born in Lenexa, Kansas, Doctor Allen was graduated from the University of Kansas School of Medicine. He served an internship at St. Joseph's Hospital, Kansas City, Mo., and at the Royal Victoria Hospital, Montreal, Canada, the latter being interrupted by his entrance into the United States Army in World War I. Assigned to the Kansas City School of Military Roentgenology, he was with the A. E. F. as a member of Base Hospital 116 and Mobile Hospital No. 9.

Following the war, Doctor Allen entered upon the private practice of radiology in Kansas City, Kans. He is radiologist to Bethany Hospital, Providence Hospital, and St. Margaret's Hospital, in that city, and is Professor of Clinical Roentgenology in the University of Kansas School of Medicine.

Doctor Allen has not limited his activities to radiology but has taken a lively interest in organized medicine. He is a Fellow of the American College of Physicians, has for many years been active in the affairs of the Kansas Medical Society, and has served as President of the Wyandotte County Medical Society and as President of the Kansas City Southwest Clinical Society. He is an honorary member of the Kansas City Academy of Medicine and active in various committees of the Medical School.

His interest in radiology has made him an energetic participant in local and national radiologic organizations. He was a member of the first class certified by the American Board of Radiology. He is a Chancellor of the American College of Radiology and Chairman of its Commission on Public Relations. He is Past-President of the Kansas Radiological Society and a member of the American Roentgen Ray Society.

Civic affairs have claimed Doctor Allen's attention to the end that he is now Chief of Emergency Medical Service under the Civilian Defense program for Kansas City, Kans., as well as participating in the Kiwanis Club, of which he is a charter member. He is a trustee of Group Hospital Service, Inc., and Surgical Care, Inc.

Doctor Allen has contributed numerous articles to the literature of radiology and has taken an active part in the programs of the medical organizations of which he is a member.

The demand for relaxation from such a busy routine is satisfied by motion picture photography and the operation of a small farm near Kansas City.

IRA H. LOCKWOOD, M.D.

LEWIS G. ALLEN, M.D.
President of the Radiological Society of North America

A Trade Journal Looks at Medicine

The August 1944 issue of the *Railroad Journal*[1] is designated "American Health Number." This remarkable issue of a trade journal should be read by all physicians interested in medical practice. We say "remarkable" because, for the first time, to our knowledge, a monthly magazine published by and for a large industrial group, devotes an entire issue to an authoritative series of articles on the problem of sickness and sickness insurance.

The tenor of the majority of the articles may be gleaned from the title of the leading editorial and the contents of a "box" at the end of the editorial section. The title of the editorial, by Nathan Smith Davis, III, M.D., of Northwestern University Medical School, is the familiar and pertinent aphorism attributed to Bishop Creighton of London: "No people do so much harm as those who go about doing good." To this group, in the United States, Dr. Davis attributes such projects as the National Health Program, the Report of the National Resources Planning Board, and the Wagner-Murray-Dingell Bill. The box at the end of the editorial section reads as follows:

Message to Employers

The sole purpose of this issue is to bring to you the story of the efforts and accomplishments of American Doctors and Hospitals—and to suggest that you give serious thought to the protection of yourself and your employees through the establishment of insurance programs similar to the ones described in this issue.

If You Don't Do It, the Government Will—at Higher Cost

The contributors to the issue include Victor G. Heiser, John R. Mannix, Louis H. Pink, Edward H. Skinner, Morris Fishbein, and numerous other well known writers on the subject of medical care. Their opinions are expressed concisely, and the volume represents an unusually convenient collection of such points of view. If any suggestion could be made for future issues of this type, it would be to include more data on *all* of the various State Medical Society sponsored plans, and to list the addresses in order that interested executives and others would know exactly where to go for information.

L. H. GARLAND
Lt. Comdr. (MC) USNR

[1] Available from Mr. Alex Brandau, Public Relations Director, The Railroad Journal, 65 East Harrison St., Chicago, Ill.

ANNOUNCEMENTS AND BOOK REVIEWS

NEBRASKA RADIOLOGICAL SOCIETY

At the meeting of the Nebraska Radiological Society held Nov. 15, the following officers were elected: F. L. Simonds, M.D., Omaha, President; Donald H. Breit, M.D., University of Nebraska Hospital, Omaha 5, Secretary-Treasurer.

VIRGINIA RADIOLOGICAL SOCIETY

The newly elected officers of the Virginia Radiological Society are: Clayton W. Eley, M.D., Norfolk, President; W. P. Gilmer, M.D., Clifton Forge, Vice-President, and E. L. Flanagan, M.D., Richmond, Secretary.

Book Reviews

METASTASES, MEDICAL AND SURGICAL. By MALFORD W. THEWLIS, M.D., Attending Specialist in General Medicine, United States Public Health Hospitals, New York City; Attending Physician, South County Hospital, Wakefield, Rhode Island; Special Consultant, Rhode Island Department Public Health; Author Care of the Aged (Geriatrics), Preclinical Medicine. Foreword by HUBERT A. ROYSTER, A.B., M.D., F.A.C.S., Honorary Chief of Surgical Service, Rex Hospital; Chief-of-Staff, St. Agnes Hospital; Consulting Surgeon, Dix Hill State Hospital, Raleigh; Fellow, American Board of Surgery. A volume of 230 pages, with 13 illustrations. Published by the Charlotte Medical Press, Charlotte, N. C., 1944. Price $5.00.

The term metastasis, while it is particularly associated with transfer through the blood or lymph stream of malignant cells from a primary focus to some distant site, is equally applicable to the movement of bacteria and to the change of location of diseases of virus origin and those due to protozoa and other parasites. All these phases of the problem are included in Doctor Thewlis's book. The work is essentially a series of outlines, preceded by a brief general introduction. Its object is to provide a ready guide to the probable secondary sites of various disease processes.

The first of the outlines has to do with Neoplasms. Here are listed the numerous types of new growth—from acanthoma to xanthomatosis—with the primary sites and the sites of metastasis given under each, the sites of predilection being italicized. The second and third outlines cover Infections and Infectious Diseases, between which the author makes a distinction. Under the latter head are included actinomycosis, amebiasis, bilharziasis, blastomycosis, cerebrospinal meningitis, echinococcus cyst, erysipelas, gonorrhea, influenza, leishmaniasis, meningitis, mumps, parasitic diseases (trypanosomiasis, malaria, filariasis), rheumatic fever, S. suipestifer infection, syphilis, trichinosis, tuberculosis, tularemia, and typhoid. The fourth of the outlines, headed Miscellany, includes a variety of conditions not covered by the other classifications, as the anemias, arthritis, endocarditis, leukemia, etc. The final outline, which covers 100 pages, or almost half the volume, is perhaps the most valuable of all. Here the organs and regions of the body are listed with the primary lesions affecting each, the metastases to which they may give rise, and the metastatic lesions by which each may be involved.

An extensive bibliography is given at the end of the book and an adequate index makes it possible to find quickly either the disease or anatomical area in which one is interested. This feature is particularly useful, as the author's classification of diseases may in some instances be open to question. A number of anatomical drawings showing the lymph drainage areas are reproduced from standard texts.

Mechanically the book suffers somewhat from wartime printing conditions, and it is unfortunate that the errors listed on the insert could not have been caught in the proof. These features, however, do not impair the value of the work for reference. It should appeal especially to the busy practitioner who wishes to refresh his memory as to the routes and sites of metastasis. It will be of value to internists, surgeons, pathologists, and roentgenologists, and, of course, to all students of medicine.

THE 1944 YEAR BOOK OF RADIOLOGY. Diagnosis, edited by CHARLES A. WATERS, M.D., Associate in Roentgenology, Johns Hopkins University; Assistant Visiting Roentgenologist, Johns Hopkins Hospital; Associate Editor, WHITMER B. FIROR, M.D., Assistant in Roentgenology, Johns Hopkins University; Assistant in Roentgenology, Johns Hopkins Hospital (on leave with the Armed Forces). Therapeutics, edited by IRA I. KAPLAN, B.Sc., M.D., Director, Radiation Therapy Department, Bellevue Hospital, New York City; Clinical Professor of Surgery, New York University Medical College. A volume of 448 pages, with 363 illustrations. Published by The Year Book Publishers, Chicago, Ill. Price $5.00.

This latest addition to the series of Year Books of Radiology follows the general plan of the earlier volumes in its presentation of abstracts of articles appearing in the world's literature during the last year, which is to say from about the middle of 1943 to the middle of 1944. It is a volume of 450 pages.

well printed and bound, and a worthy addition to any medical library.

As the editors point out, the year was a particularly difficult one for such a project. In spite of this, the volume compares favorably with those of past years. The literature—with unavoidable geographical limitations—is well covered, and the abstracts are good, giving the essential content of the articles in fairly full detail. The reproduction of numerous well chosen illustrations adds greatly to the value of the text. Under the two main divisions of Diagnosis and Therapy, the material is classified on an anatomical basis, and a comprehensive index is appended.

The book is interesting and instructive throughout and is especially helpful now, when so much must be done in so little time. It is recommended without qualification.

THE PRACTICE OF MEDICINE. By JONATHAN CAMPBELL MEAKINS, M.D., LL.D., Brigadier, Deputy Director General of Medical Services, Royal Canadian Army Medical Corps; Professor of Medicine and Director of the Department of Medicine, McGill University; Physician-in-Chief, Royal Victoria Hospital, Montreal; Formerly Professor of Therapeutics and Clinical Medicine, University of Edinburgh; Fellow of the Royal Society of Edinburgh; Fellow of the Royal Society of Canada; Fellow of the Royal College of Physicians, London; Fellow of the Royal College of Physicians, Edinburgh; Honorary Fellow of the Royal College of Surgeons, Edinburgh; Fellow of the Royal College of Physicians, Canada; Fellow of the American College of Physicians; Honorary Fellow of the Royal Society of Medicine. A volume of 1,444 pages, with 517 illustrations, including 48 in color. Published by the C. V. Mosby Co., St. Louis, Mo. Fourth Edition, 1944. Price $10.00.

The present edition of Meakins's well known *Practice of Medicine* represents a considerable revision over the edition of 1940, new material having been added to keep pace with advances both in civilian practice and in military medicine. The current interests of the author, as Brigadier, Deputy Director General of Medical Services of the Royal Canadian Army Medical Corps, are reflected in the inclusion in a text on internal medicine of such conditions as immersion foot, blast injuries, crush syndrome, and other states which have become more common in wartime. All of the general features of the previous edition are retained or amplified. The section on the use of the sulfonamides is thoroughly adequate for a general text, and additional consideration of chemotherapy is given under the specific diseases in which it is indicated. Penicillin receives brief mention.

A unique feature is the illustrative material included in this book. Of the 517 illustrations, 186 are reproductions of roentgenograms, well selected for their teaching value. The present-day importance of radiography in diagnosis is well correlated with the clinical picture in diseases of the various systems.

In line with modern thought, added emphasis is placed on functional disturbances and psychosomatic medicine. The importance of prophylaxis over therapy—positive health as opposed to negative health or disease—is stressed.

Each section is followed by an adequate bibliography, and a 50-page index makes the comprehensive contents of this text readily accessible.

THE URINARY TRACT. A HANDBOOK OF ROENTGEN DIAGNOSIS. By H. DABNEY KERR, M.D., Professor of Radiology, State University of Iowa College of Medicine, and CARL L. GILLIES, M.D., Associate Professor of Radiology, State University of Iowa College of Medicine. A volume of 320 pages, with numerous illustrations. Published by The Year Book Publishers, Inc., Chicago. Price $5.50.

This is the third of a projected six-volume series of handbooks on roentgen diagnosis and follows essentially the form of the preceding volumes. It is actually an atlas containing many illustrations and streamlined clinical and roentgenological text of unusual clarity.

The authors have divided the book into sections on the kidney, ureter, bladder, and urethra. Under each section a fairly uniform pattern is followed. A general description is given of the lesion under consideration, followed by a group of excellent illustrations, each of which is clearly described on the opposite page. These illustrations are unretouched and the reduction is uniform throughout, 37 per cent of actual size. Many helpful hints regarding differential diagnosis are included both in the text and illustrations. A bibliography is appended.

This is an excellent handbook for students and roentgenologists and can be highly recommended. It is concise, lucid, and surprisingly complete for its size.

RADIOLOGICAL SOCIETIES OF NORTH AMERICA

Editor's Note.—Will secretaries of societies please cooperate by sending information to Howard P. Doub, M.D., Editor, Henry Ford Hospital, Detroit 2, Mich.

UNITED STATES

Radiological Society of North America.—Secretary, D. S. Childs, M.D., 607 Medical Arts Building, Syracuse 2, N. Y.

American Roentgen Ray Society.—Secretary, Harold Dabney Kerr, M.D., Iowa City, Iowa.

American College of Radiology.—Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago 11, Ill.

Section on Radiology, American Medical Association.—Secretary, U. V. Portmann, M.D., Cleveland Clinic, Cleveland 6, Ohio.

ARKANSAS

Arkansas Radiological Society.—Secretary, J. S. Wilson, M.D., Monticello. Meets every three months and annually at meeting of State Medical Society.

CALIFORNIA

California Medical Association, Section on Radiology.—Secretary, Earl R. Miller, M.D., University of California Hospital, San Francisco, Calif.

Los Angeles County Medical Association, Radiological Section.—Secretary, Roy W. Johnson, M.D., 1407 South Hope St., Los Angeles. Meets second Wednesday of each month at County Society Building.

Pacific Roentgen Society.—Secretary, L. Henry Garland, M.D., 450 Sutter St., San Francisco. Meets annually during meeting of California Medical Association.

San Diego Roentgen Society.—Secretary, Henry L. Jaffe, M.D., Naval Hospital, Balboa Park, Calif. Meets first Wednesday of each month.

San Francisco Radiological Society.—Secretary, Martha Mottram, M.D., Suite 1789, 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., in Toland Hall, University of California Hospital, from January to June; at Lane Hall, Stanford University Hospital, July to December.

COLORADO

Denver Radiological Club.—Secretary, A. Page Jackson, Jr., M.D., 304 Republic Bldg., Denver 2. Meetings third Friday of each month at the Denver Athletic Club.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Secretary, Max Climan, M.D., 242 Trumbull St., Hartford 3. Meetings bimonthly, second Thursday.

FLORIDA

Florida Radiological Society.—Secretary-Treasurer Charles M. Gray, 306 Citizens Bldg., Tampa 2.

GEORGIA

Georgia Radiological Society.—Secretary-Treasurer, James J. Clark, M.D., 478 Peachtree St., N. E., Atlanta 3. Meetings twice annually, in November and at the annual meeting of State Medical Association.

ILLINOIS

Chicago Roentgen Society.—Secretary, Fay H. Squire, M.D., 1753 W. Congress St., Chicago 12. Meets at the Palmer House, second Thursday of October, November, January, February, March, and April.

Illinois Radiological Society.—Secretary-Treasurer, William DeHollander, M.D., St. Johns' Hospital, Springfield. Meetings quarterly by announcement.

Illinois State Medical Society, Section on Radiology.—Secretary, Frank S. Hussey, M.D., 250 East Superior St., Chicago 11.

INDIANA

The Indiana Roentgen Society.—Secretary-Treasurer, Harold C. Ochsner, M.D., Methodist Hospital, Indianapolis 7. Annual meeting in May.

IOWA

The Iowa X-ray Club.—Secretary, Arthur W. Erskine, M.D., Suite 326 Higley Building, Iowa City. Holds luncheon and business meeting during annual session of Iowa State Medical Society.

KENTUCKY

Kentucky Radiological Society.—Secretary-Treasurer, Sydney E. Johnson, 101 W. Chestnut St., Louisville.

LOUISIANA

Louisiana Radiological Society.—Secretary-Treasurer, Johnson R. Anderson, M.D., North Louisiana Sanitarium, Shreveport. Meets annually at same time as State Medical Society.

Shreveport Radiological Club.—Secretary-Treasurer, R. W. Cooper, 940 Margaret Place. Meetings monthly on the second Wednesday, at offices of members.

MARYLAND

Baltimore City Medical Society, Radiological Section.—Secretary, Walter L. Kilby, M.D., 101 W. Read St., Baltimore 1. Meets third Tuesday of each month.

MICHIGAN

Detroit X-ray and Radium Society.—Secretary-Treasurer, E. R. Witwer, M.D., Harper Hospital, Detroit 1. Meetings first Thursday of each month from October to May, inclusive, at Wayne County Medical Society club rooms, 4421 Woodward Ave., Detroit.

Michigan Association of Roentgenologists.—Secretary-Treasurer, E. M. Shebesta, M.D., 1429 David Whitney Bldg., Detroit. Meetings quarterly by announcement.

MINNESOTA

Minnesota Radiological Society.—Secretary, A. T. Stenstrom, M.D., Minneapolis General Hospital, Minneapolis 26. Meetings quarterly.

MISSOURI

Radiological Society of Greater Kansas City.—Secretary, Arthur B. Smith, M.D., 306 E. 12th St., Kansas City, Mo. Meetings last Thursday of each month.

The St. Louis Society of Radiologists.—Secretary, E. W. Spinzig, M.D., 2646 Potomac St. Meets on fourth Wednesday of each month except June, July, August, and September, at a place designated by the president.

NEBRASKA

Nebraska Radiological Society.—Secretary-Treasurer, Donald H. Breit, M.D., University of Nebraska Hospital, Omaha 5. Meetings third Wednesday of each month at 6 P.M. in either Omaha or Lincoln.

NEW ENGLAND

New England Roentgen Ray Society (Maine, New Hampshire, Vermont, Massachusetts, and Rhode Island).—*Secretary-Treasurer,* George Levene, M.D., Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday at Boston Medical Library.

NEW JERSEY

Radiological Society of New Jersey.—Secretary, H. R. Brindle, M.D., 501 Grand Ave., Asbury Park. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called by president.

NEW YORK

Associated Radiologists of New York, Inc.,—Secretary, William J. Francis, M.D., 210 Fifth Ave., New York City. Regular meetings the first Monday evening of the month in March, May, October, and December.

Brooklyn Roentgen Ray Society.—Secretary-Treasurer, Leo Harrington, M.D., 880 Ocean Ave., Brooklyn 26. Meets fourth Tuesday of every month, October to April.

Buffalo Radiological Society.—Secretary-Treasurer, Joseph S. Gianfranceschi, M.D., 610 Niagara St., Buffalo 1. Meetings second Monday evening each month. October to May, inclusive.

Central New York Roentgen Ray Society.—Secretary-Treasurer, Carlton F. Potter, M.D., 425 Waverly Ave., Syracuse 10. Meetings are held in January, May, and October, as called by Executive Committee.

Long Island Radiological Society.—Secretary, Marcus Wiener, M.D., 1430 48th St., Brooklyn 19. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

New York Roentgen Society.—Secretary, Ramsay Spillman, M.D., 115 E. 61st St., New York 21, N. Y.

Rochester Roentgen-ray Society.—Secretary, Murray P. George, M.D., 260 Crittenden Blvd., Rochester 7. Meetings at convenience of committee.

NORTH CAROLINA

Radiological Society of North Carolina.—Secretary-Treasurer, Major I. Fleming, M.D., 404 Falls Road, Rocky Mount. Meeting with State meeting in May, and meeting in October.

NORTH DAKOTA

North Dakota Radiological Society.—Secretary, L. A. Nash, M.D., St. John's Hospital, Fargo. Meetings by announcement.

OHIO

Ohio Radiological Society.—Secretary, Henry Snow, M.D., 1061 Reibold Bldg., Dayton 2. Next meeting will be held at the time and place of the annual meeting of the Ohio State Medical Association.

Cleveland Radiological Society.—Secretary-Treasurer, Don D. Brannan, M.D., 11311 Shaker Blvd., Cleveland 4. Meetings at 6:30 P.M. on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*Secretary-Treasurer,* Samuel Brown, M.D., 707 Race St., Cincinnati 2. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—Secretary-Treasurer, L. E. Wurster, M.D., 416 Pine St., Williamsport 8. The Society meets annually.

The Philadelphia Roentgen Ray Society.—Secretary, Robert P. Barden, M.D., 3400 Spruce St., Philadelphia 4. Meetings held first Thursday of each month at 8:15 P.M., from October to May, in Thomson Hall, College of Physicians, 21 S. 22d St., Philadelphia.

The Pittsburgh Roentgen Society.—Secretary-Treasurer, Lester M. J. Freedman, M.D., 4800 Friendship Ave., Pittsburgh 24, Pa. Meetings are held on the second Wednesday of each month at 4:30 P.M., from October to June, at the Pittsburgh Academy of Medicine, 322 N. Craig St.

ROCKY MOUNTAIN STATES

Rocky Mountain Radiological Society (North Dakota South Dakota, Nebraska, Kansas, Texas, Wyoming Montana, Colorado, Idaho, Utah, New Mexico).—*Secretary,* A. M. Popma, M.D., 220 North First St. Boise, Idaho.

SOUTH CAROLINA

South Carolina X-ray Society.—Secretary-Treasurer Robert B. Taft, M.D., 103 Rutledge Ave., Charleston 16.

TENNESSEE

Memphis Roentgen Club.—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

Tennessee Radiological Society.—Secretary-Treasurer, J. Marsh Frère, M.D., 707 Walnut St., Chattanooga. Meeting annually with State Medical Society in April.

TEXAS

Dallas-Fort Worth Roentgen Study Club.—Secretary, X. R. Hyde, M.D., Medical Arts Bldg., Fort Worth, Texas. Meetings on third Monday of each month, in Dallas in the odd months and in Fort Worth in the even months.

Texas Radiological Society.—Secretary-Treasurer, Asa E. Seeds, Baylor Hospital, Dallas.

VIRGINIA

Virginia Radiological Society.—Secretary, E. Latané Flanagan, M.D., 215 Medical Arts Bldg., Richmond 19.

WASHINGTON

Washington State Radiological Society.—Secretary-Treasurer, Thomas Carlile, M.D., 1115 Terry Ave., Seattle Meetings fourth Monday of each month, October through May, at College Club, Seattle.

WISCONSIN

Milwaukee Roentgen Ray Society.—Secretary-Treasurer C. A. H. Fortier, M.D., 231 W. Wisconsin Ave., Milwaukee 3. Meets monthly on second Monday at the University Club.

Radiological Section of the Wisconsin State Medical Society.—Secretary, Russell F. Wilson, M.D., Beloit Municipal Hospital, Beloit. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society, in September.

University of Wisconsin Radiological Conference.—Secretary, E. A. Pohle, M.D., 1300 University Ave. Madison 6, Wis. Meets every Thursday from 4 to 5 P.M., Room 301, Service Memorial Institute.

CANADA

La Société Canadienne-Française d'Electrologie et de Radiologie Médicales.—General Secretary, Origène Dufresne, M.D., Institut du Radium, Montreal. Meetings are held the third Saturday of each month, generally at the Radium Institute, 4120 East Ontario Street, Montreal; sometimes, at homes of members.

CUBA

Sociedad de Radiología y Fisioterapia de Cuba.—Offices in Hospital Mercedes, Havana. Meetings are held monthly.

ABSTRACTS OF CURRENT LITERATURE

ROENTGEN DIAGNOSIS

The Head and Neck

The Chest

The Digestive System

The Skeletal System

The Genito-Urinary Tract

Parasites

RADIOTHERAPY

Neoplasms

EXPERIMENTAL STUDIES

ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Roentgenological Findings in Bilateral Symmetrical Thinness of the Parietal Bones (Senile Atrophy): Report of a Case with a Review of the Literature. Angus K. Wilson. Am. J. Roentgenol. **51:** 685–696, June 1944.

A case of bilateral symmetrical thinness of the parietal bones is presented in detail and a general review of the literature is given with a bibliography of sixty-seven references. It is probable that the condition was known to the ancients, since many examples taken from Egyptian tombs have been described. The first modern description is ascribed to Köhler in 1786. The characteristic location of the thinned areas is between the sagittal suture and the parietal prominence. Characteristically, there is a crest-like ridge of intervening bone centered on the sagittal suture which separates the parietal depressions. Frequently, there is a shallow groove-like depression of the sagittal crest.

Two chief forms have been described: (1) a roughly triangular or quadrilateral flattened depressed area and (2) a trough-like depression running longitudinally along both sides of the sagittal suture. The latter type may extend into the frontal and occipital areas. Pathologically, there is no sharp line of demarcation between the depression and the adjacent normal external tables; the margins shelve gradually into the thinned area. The floor of the depression may be of parchment-like thinness, extremely fragile, and translucent.

Many theories have been advanced in an attempt to explain this thinning of the parietal bones. By the majority of authors it is considered an atrophic change, but explanation as to the cause of the atrophy varies widely. The views of numerous students of the subject are presented.

Roentgen diagnosis of the condition and differentiation from disease processes are based on the finding of (1) a symmetrical bilateral localized involvement with (2) smooth, regular margins, (3) absence of a surrounding zone of new bone formation, (4) lack of evidence of malignant lesions elsewhere in the body, and (5) absence of pain or tenderness. The author was able to find only one other case published in the American literature with roentgenologic findings (Moore: J. Missouri M. A. **26:** 396, 1929), but in a footnote refers to a recent article by Camp and Nash (Radiology **42:** 42, 1944) which was published subsequent to the preparation of his paper. L. W. PAUL, M.D.

New Light on the Origin of Craniolacunia. J. Blair Hartley and C. W. F. Burnett. Brit. J. Radiol. **17:** 110–114, April 1944.

A case of partial or circumscribed craniolacunia or lacunar skull with hydrocephalus, in a stillborn fetus, is reported. The skull showed marked lacunar changes in the anterior halves of the cranial bones centrally, while the peripheral and posterior portions and the parietal bones were normal in this respect. The squamous portion of the occipital bone was strikingly expanded.

This case, which is the first of partial or circumscribed craniolacunia to be recorded, is of special interest in relation to the etiology of the condition. The authors examine the three most commonly held theories in the light of their observations. (1) The theory of a pressure effect due to an internal hydrocephalus would not seem to hold here, in view of the localized character of the changes. (2) While a developmental chromosomal defect might enter into consideration, observations in other cases, indicating that the condition has a tendency to disappear with increasing age, are opposed to this view, since such developmental defects and deformities invariably persist. (3) The third etiologic theory appears more likely, namely that this anomaly results from some hormonal or dietary deficiency during pregnancy. Rats receiving a deficient diet have been shown to produce offspring with congenital skull defects and rib deformities (Warkany and Nelson: Am. J. Roentgenol. **47:** 889, 1942); craniolacunia is often found in association with other skeletal defects, chiefly in membranous bones; finally, the condition is observed only in children of the poorer classes.

SYDNEY J. HAWLEY, M.D.

Tuberous Sclerosis. A. T. Ross and W. W. Dickerson. Arch. Neurol. & Psychiat. **50:** 233–257, September 1943.

In this rather lengthy article, the various features of the congenital hereditary or familial entity known as tuberous sclerosis are discussed in detail. The basic characteristics of this developmental tissue dysplasia are of ectodermal origin, but defective development and tumor formation are frequently identified elsewhere.

Clinically, the outstanding findings are adenoma sebaceum on the face, retinal tumors, mental deficiency, and convulsions. Neurological changes are usually minimal despite the occurrence of numerous nodular sclerotic areas throughout the central nervous system and viscera.

Roentgenograms of the skull may show multiple small discrete areas of calcification throughout the brain substance, particularly in the region of the sella turcica, the basal ganglia, and the choroid plexuses. Additional round or oval areas of increased density may be found within the calvarium. Pneumoencephalograms usually show some degree of generalized brain atrophy and occasionally yield evidence of the one pathognomonic sign of tuberous sclerosis, *viz.*, intraventricular tumors having the appearance of wax candle gutterings.

Roentgenograms of the hands may show cystic areas of rarefaction in the metacarpals and phalanges, and osteoporosis. Polydactylism also may be present.

DEPARTMENT OF ROENTGENOLOGY
UNIVERSITY OF MICHIGAN (J. H.)

Tumor of the Acoustic Nerve within the Petrous Bone. Leo J. Adelstein and Frank M. Anderson. Arch. Neurol. & Psychiat. **51:** 268–270, March 1944.

Most acoustic neuromas arise within the petrous bone or just outside the internal auditory meatus, usually growing in the direction of least resistance, to occupy the cerebellopontine angle. The case reported in this article, in a girl of fifteen, is unique in that the tumor was confined entirely within the petrous bone, yet grew to such proportions that it produced cerebellar signs, slight impairment of trigeminal nerve function, diminution of the deep reflexes on the opposite side of

the body, and increase in intracranial pressure. Roentgen exposures in the Towne and Stenvers projections showed extensive erosion of the right internal acoustic meatus and the ridge of the right petrous bone. Gradual onset of tinnitus and deafness in the right ear had been observed over a period of six years. Operative removal of the tumor was followed three months later by a spinal accessory-facial nerve anastomosis with excellent clinical results.

DEPARTMENT OF ROENTGENOLOGY
UNIVERSITY OF MICHIGAN (J. H.)

Cholesteatoma with Fistula into the Labyrinth. Report of a Case in Which the Roentgenologic Findings Were Confusing. Hans Von Leden and Henry L. Williams. Arch. Otolaryng. **39:** 432–433, May 1944.

A 37-year-old woman complained of intermittent discharge from the left ear and dizziness. The discharge had been present for four years and the dizziness for fourteen months. Examination revealed a dry ear with a medium-sized attic fistula. The drum membrane was covered with hard crusts and could not be fully visualized. The right drum membrane was thickened and somewhat retracted but otherwise normal. Tuning fork tests and an audiogram revealed moderate conduction deafness on the left side. There was spontaneous nystagmus on looking to both sides, and the fistula test was mildly positive on the left.

Roentgenographic examination of the mastoid regions revealed no abnormality on the left side except that the cells were small. The right mastoid process, however, was reported as being markedly sclerotic with an irregular, poorly defined area of rarefaction in the epitympanic region, which was interpreted as a cholesteatoma. The roentgen examination was repeated to make certain that the two sides were properly identified on the film.

At operation, a large cholesteatoma was found in the *left* epitympanum. It had eroded into the anterior part of the horizontal semicircular canal and produced a large fistula. The roentgen findings on the *right* side were now interpreted as representing an ancient quiescent lesion.

This case demonstrates that a laboratory test, such as a roentgenographic examination, may be misleading and that, when laboratory findings conflict with clinical findings, the greater weight should be given to the latter.

Carcinoma of the Thyroid Gland with a Solitary Metastasis to the Skull. Hollis L. Albright. New England J. Med. **230:** 573–576, May 11, 1944.

A 52-year-old female had a moderately firm, nontender mass measuring 2.5 × 1.0 cm. in the right frontal area. Roentgen examination showed a defect involving both tables of the skull with slight secondary condensation of adjacent bone. A hard nodule was also found in the right lobe of the thyroid. The patient was operated upon and the thyroid nodule was removed. The mass in the right frontal area was also removed. Both specimens were found to be thyroid carcinoma. The patient was well, without evidence of further metastasis or recurrence, two and a half years later, justifying the surgical removal of both the primary and the metastatic malignant growth.

JOHN B. MCANENY, M.D.

Radiography of the Neck of the Condyle. A. Porter S. Sweet, U. S. Nav. M. Bull. **42:** 1135–1139, May 1944.

A survey of the literature reveals numerous technics that can be used for examination of the condyle of the mandible, but these appear to have been developed primarily for examination of the temporomandibular joint and are often unnecessarily complicated. The author describes a simple technic, using a dental x-ray unit, based on a modification of the Schlegel method. This produces a satisfactory view of the neck of the condyle at the sacrifice of joint clarity.

The patient is seated in a dental chair with his head so placed that the interpupillary line of the eyes and an imaginary line from the ala of the nose to the tragus of the ear will be parallel to the floor. A cassette, which should rest against the cheek and ear securely so that no rocking will occur, is so positioned that the image of the condyle will be as near as possible to the center of the film. A large cork is placed between the incisors to bring the condylar neck forward as well as to insure against motion. The dental cone is removed from the tube-head and the tube is placed in contact with the opposite condylar neck so that the central ray passes directly through the neck of both condyles. Exposure factors must be determined for the particular machine in use.

LESTER M. J. FREEDMAN, M.D.

THE CHEST

Primary Atypical Pneumonia. An Analysis of 738 Cases Occurring During 1942 at Scott Field, Ill. Charles A. Owen. Arch. Int. Med. **73:** 217–231, March 1944.

In 1942, at the Station Hospital, Scott Field, 799 patients were treated for pneumonia. Twenty-four had typical lobar pneumonia and 775 bronchopneumonia. Among the latter were 738 patients with clinical and laboratory findings suggestive of a non-bacterial cause.

Roentgenography is the most important, but not the sole means of diagnosis of atypical pneumonia. In general, the roentgen findings in this series were those which have become well established for this condition. A predilection for involvement of the lower lobe was marked, occurring in 612 cases, with a slight but definite predominance of the left lower lobe. Extensions of the pneumonic process occurred in 64 cases, with involvement of the opposite lung in 40.

The diagnosis of pneumonia was made in 15 cases with no definite roentgen changes beyond accentuation of truncal markings; this seemed justified from the clinical course and findings. In 30 cases the findings in the chest suggested pneumonia, while the initial films appeared normal, though the later ones were confirmatory. The detection of pulmonary signs prior to roentgenographic evidence is in sharp contrast to the usual minimal findings in the early stages. In 14 cases in which both the roentgen and thoracic findings were negative early but subsequently positive, pneumonia was suspected on the basis of the history and the general appearance of the patient.

Serious complications among the 738 cases of atypical pneumonia were rare; there were no fatalities. The disease showed epidemic tendencies during the late summer and fall when common diseases of the respiratory tract were at a minimum. Prolonged convalescence is the rule. From a military standpoint the time

lost is significant. Over 20,000 man-days were lost at Scott Field during 1942 from atypical pneumonia.

Atypical Pneumonia Simulating Pulmonary Tuberculosis. J. S. Yoskalka. Am. Rev. Tuberc. **49:** 408–413, May 1944.

In recent years it has become apparent that atypical pneumonia can produce lesions which at times are indistinguishable from pulmonary tuberculosis. Seven cases of upper lobe atypical pneumonia were reviewed in order to determine, if possible, whether any diagnostic criteria could be established for this disease. The most common roentgen finding was an increase in bronchial markings manifested by linear streaking densities with superimposed mottled shadows. This process was found to be most pronounced at the hilum and to spread outwards in a fan-like manner toward the periphery. The other type of finding was an area of increased density in the parenchyma of the lung relatively uniform throughout, resembling the shadow seen in early pleural effusion. In some instances, evidence of atelectasis was present. There was a wide divergence of roentgenologic findings in the various cases at different times, and the authors feel that a definite differential diagnosis cannot be made from a single roentgenogram. Stereoroentgenograms are of value in diagnosis in doubtful cases. If the apical lesions fail to disappear within twenty days following the onset of the disease, the possibility of pulmonary tuberculosis should be entertained. This necessitates thorough investigation for tubercle bacilli, including a study of sputum and gastric contents and guinea-pig inoculation. One case is reported which was diagnosed as atypical pneumonia and which later proved to be tuberculosis. L. W. PAUL, M.D.

Bagasse Disease of the Lungs. W. A. Sodeman and R. L. Pullen. Arch. Int. Med. **73:** 365–374, May 1944.

Seven cases of bagasse disease of the lungs have previously been recorded. The authors summarize the findings in these cases and in 11 of their own. Two histories are presented in detail. All of the patients were men, with an average age of twenty-seven. Six patients were white, 5 were Negroes. The length of exposure to bagasse dust before symptoms arose was known in 8 cases and varied from three weeks to two years. A clear-cut history of exposure for only three weeks to two months was obtained in 3 of these cases.

The symptomatic picture was variable but showed several rather constant features. Cough and dyspnea were early and important symptoms, occurring in all cases. Dyspnea was almost invariably the presenting complaint; characteristically it appeared suddenly and became sufficiently severe within a few days to force the patient to rest. Examination of the chest showed nothing striking. Impaired resonance and diminished breath sounds were observed in 4 cases, usually in the bases of the lungs posteriorly. Roentgen examination of the chest revealed what was uniformly described as a miliary mottling throughout both lungs, most dense in the hilar areas. These areas in general had a ground-glass appearance. In only one case were the apexes involved. Ten of the 11 patients had leukocyte counts above 10,000, averaging approximately 13,000. In 7 cases differential counts indicated polymorphonuclear leukocytosis, the percentage of polymorphonuclear cells varying from 73 to 90. Eosinophils averaged 3.5 per cent. In 5 cases the sedimentation rate showed a definite increase.

Treatment consisted of rest in bed during the acute stage of the disease and palliative medication and procedures. The stay in the hospital varied from nine to ninety-three days. A follow-up investigation of 6 cases over periods of four months showed perfectly clear roentgenograms of the chest in 5 and a residual which appeared to be clearing in one.

A fungus, an allergic reaction, tuberculosis, and pneumoconiosis have all been suggested as possible causes for this condition. Histologic study of involved areas of the lung indicates the presence of bagasse dust with a severe and unusual cellular reaction, the nature of which has not yet been established.

Pulmonary Hemosiderosis in a Six Year Old Boy: Clinical and Pathologic Report. J. D. Pilcher and Oliver Eitzen. Am. J. Dis. Child. **67:** 387–392, May 1944.

A 5-year-old undernourished white boy was hospitalized because of fatigability, muscular weakness, and anemia of three months' duration. On admission, examination of the blood showed 1,880,000 red cells, 19,000 white cells, and 20 per cent hemoglobin, with severe hypochromia, microcytosis, anisocytosis, and poikilocytosis. Tuberculin and Wassermann tests were negative. Roentgenograms of the chest showed an unusual diffuse, mottled infiltration, most dense at the hila, radiating throughout both lung fields almost to the periphery, "resembling miliary tuberculosis that had been flattened or squashed." The patient gave no history of previous lung disease, cough, or expectoration.

Several transfusions were given and the patient was discharged at the end of one month with a red cell count of 3,800,000, 16,000 white cells, and 70 per cent hemoglobin. The red cells had returned to normal, platelets and reticulocytes were abundant, fragility tests and clotting time were normal, but the bleeding time was slightly prolonged (six minutes) and the icteric index was 16 (normal 4–6). Re-examination of the chest showed no change. A diagnosis of chronic interstitial pneumonitis was made.

During the ensuing months the blood picture became normal, but progressively severe signs and symptoms of pulmonary fibrosis developed, including clubbing and cyanosis of the fingers and toes, breathlessness, and distinct enlargement of the pulmonary conus, evident clinically and roentgenologically. Death occurred about eighteen months after the onset of symptoms, from cardiac decompensation following an upper respiratory infection. The blood picture had remained normal in the interval.

While a diagnosis of hemosiderosis had been suggested roentgenographically, this was discounted clinically because of the absence of physical signs and the complete lack of sputum, bloody or otherwise. At autopsy, however, the alveolar and capillary walls were found to be variably thickened by fibrous tissue, and golden brown pigment was discovered free in the alveolar spaces and walls as well as in the numerous macrophages present. Several hilar nodes also contained pigment and phagocytic cells. Capillary hyperemia and focal hemorrhages were noted. Numerous stain tests showed little elastic tissue, a predominance of fibrous tissue, reticulin, iron pigment, and calcium salts. A polarizing microscope revealed no silica.

The pathogenesis of the pulmonary and vascular fibrosis is discussed with particular consideration as to which was primary, but no conclusions are drawn. The opacities in the films were attributable to hemosiderin, which is a radiopaque decomposition product of hemoglobin from extravasated blood (Wells, H. G.: Chemical Pathology, 4th ed., Philadelphia, W. B. Saunders Co., 1920). The pigmentation was not, however, considered a primary cause of the disease, as it has been found in tissue without fibrosis. Widespread deposition of the pigment may occur from a focal hemorrhage, since hemosiderin is relatively insoluble and is only slowly removed from the tissues.

The roentgen illustrations show the progressive cardiac enlargement and the hilar adenopathy in the case reported but do not demonstrate the pulmonary infiltrations. The author compares his case to that of Anspach (Am. J. Roentgenol. **41:** 592, 1939), which was strikingly similar pathologically but showed some clinical differences. LESTER M. J. FREEDMAN, M.D.

Pneumothorax Due to Metastatic Sarcoma. Report of Two Cases. T. F. Thornton, Jr., and Robert T. Bigelow. Arch. Path. **37:** 334–336, May 1944.

Spontaneous pneumothorax in the presence of a primary neoplasm of the lung is uncommon. In the presence of a metastatic tumor of the lung it is extremely rare. Two cases of spontaneous pneumothorax due to metastatic sarcoma are reported. In one the primary growth was a spindle-cell fibrosarcoma of the flexor tendon of the thumb, in the other an osteogenic sarcoma of the femur.

A Tumor Occurring in the Superior Pulmonary Sulcus. Irving Imber. Am. J. M. Sc. **207:** 654–660, May 1944.

Pancoast believed that the superior pulmonary sulcus tumor was extrapulmonary and extrapleural in origin. Others believe that most of the tumors so designated are bronchiogenic in origin, and that any tumor or inflammatory mass arising in the apex of the lung or in the pulmonary sulcus could produce the same syndrome. In the case recorded here a superior pulmonary sulcus tumor syndrome was produced by a tumor which was definitely extra-pulmonary. The clinical and radiographic findings were characteristic: (1) pain in the back, radiating to the arm, followed by atrophy of the muscles of the hand, (2) cough, (3) loss of weight, (4) Horner's syndrome, and (5) a mass in the apex of the hemithorax. The upper ribs and dorsal vertebrae and the sternum quickly became eroded. Later distant metastases appeared.

A superior pulmonary sulcus tumor was found at autopsy. It had invaded the sternum, the 1st and 2d ribs and dorsal vertebrae, the brachial plexus, and sympathetic ganglion, and had metastasized to the skin, peritoneum, and adrenals. Microscopically, the tumor was definitely extra-pulmonary. Since the actual source could not be determined, Pancoast's theory of origin from the precervical sulcus deserves consideration. BENJAMIN COPLEMAN, M.D.

Four-Inch Packing Nail in the Lung: Case Followed for Thirteen Years. J. Blair Hartley. Brit. J. Radiol. **17:** 157–159, May 1944.

An adult patient with a four-inch nail in the right lung, embedded in the middle lobe bronchus, was followed for thirteen years without evidence of lung changes. During this period he had an attack of pneumonitis involving the right base, from which he recovered. SYDNEY J. HAWLEY, M.D.

THE DIGESTIVE SYSTEM

Organic Upper Gastro-Intestinal Disease at an Advance Base. John H. L. Heintzelman and Harold W. Jacox. U. S. Nav. M. Bull. **42:** 1035–1037, May 1944.

At an advance naval base in the South Pacific, the case histories and films of 200 consecutive patients receiving x-ray examinations of the gastro-intestinal tract were studied to determine the incidence of organic disease and any diagnostic aids that would limit examinations to those patients likely to yield positive findings.

The most common chief complaint was epigastric pain or distress. Complete histories were obtained for all but a few out-patients and were classified as typical for ulcer if the pain was in relation to meals, with relief by food or medication, or if hematemesis were present with or without pain. All other histories were considered atypical.

The type of history and age group are considered of definite value in determining the need of a gastro-intestinal series. Of the 200 patients, 64 gave typical histories and 22 had demonstrable ulcers. Of these 22 patients, 16, or 73 per cent, had typical histories. Of the 200 patients examined, 101 were under thirty years of age; 17 of the 22 patients with ulcer were older than thirty years.

Service at home or abroad apparently has little effect on the production of ulcer, since 80 of 124 patients with negative x-ray findings and 15 of the 22 with ulcer had symptoms while in civil life.

A plea is made for more careful study and observation of patients before gastro-intestinal series are ordered. The presence of psychoneurosis, malaria, hookworm, or other conditions may become apparent, either nullifying the need of these examinations or demanding transfer of the patient to a mainland hospital, where x-ray studies can be made if deemed necessary. LESTER M. J. FREEDMAN, M.D.

Surgical Treatment of Esophageal Atresia and Tracheoesophageal Fistulas. Wm. E. Ladd. New England J. Med. **230:** 625–637, May 25, 1944.

The various types of esophageal atresia and tracheoesophageal fistulas are diagrammed and described. The diagnosis is suspected when a newborn infant has an excess of saliva and possibly a cyanosis. There may be immediate vomiting of the feedings. Examination of the chest may disclose moist râles from aspirated saliva. Abdominal examination may reveal distention with tympany or complete flatness, according to the type of malformation. With these findings the next step is to insert a small catheter into the esophagus. Obstruction encountered 10 to 12 cm. from the lips, practically establishes a diagnosis of atresia. This, however, should be checked fluoroscopically, with a small amount of iodized oil, but never barium. Roentgenograms are reproduced showing the failure of the catheter to pass beyond the point of obstruction and demonstrating, also, distention of the stomach and intestines.

Postmortem examinations show that there are fre-

quently one or several accompanying congenital abnormalities in these patients.

Various surgical procedures for dealing with this abnormality are discussed and new methods that have proved successful are advocated. The outlook is not entirely hopeless. JOHN B. MCANENY, M.D.

Volvulus and Incarceration of Stomach in a Diaphragmatic Hernia with Complete Gastric Obstruction. Operative Recovery with Obliteration of Hernial Sac by Tamponade. Martin G. Vorhaus and DeWitt Stetten. Gastroenterology **2:** 307–315, May 1944.

A case of left diaphragmatic hernia is reported. Attacks of pressure, apparently induced as a result of conscious or subconscious emotional reactions and relieved by spontaneous or induced belching or vomiting, finally terminated in a volvulus of the distal half of the stomach, with rotation anteriorly and upwards. The subsequent incarceration of the antrum in the left hernial sac, with complete kinking, produced total acute gastric obstruction, as shown by roentgenograms.

At operation, the volvulus of the stomach was reduced without much difficulty, and in addition a pouch of the fundus of the stomach adjacent to the cardia, found in the hernial sac, was withdrawn. Because of the patient's critical condition and the inaccessibility of the hernial ring, a method of obliteration of the hernial sac by tamponade was employed.

Twenty days following the operation, one of the tampons was removed and a catheter was inserted about 8 inches into the drainage tract. The following day hippuran was injected through the cavity previously occupied by the incarcerated stomach. About 40 c.c. of hippuran was required to fill the cavity, which measured about 7 cm. in diameter. A roentgenogram showed all of the stomach wall below the diaphragm. Six days later the remaining tampons were removed. The catheter was left in place and x-ray studies were continued. These studies revealed a progressive and practically complete obliteration of the hernial cavity.

Roentgenograms are reproduced.

Primary Carcinoma of the Jejunum and the Ileum. P. G. Boman. Ann. Int. Med. **20:** 779–788, May 1944.

Carcinoma of the small bowel comprises from 0.47 per cent to 6.0 per cent of all carcinomas of the gastro-intestinal tract, according to different reports. Ewing's estimate of 3.0 per cent is probably correct. Adenocarcinoma is the predominant type, accounting for over 90 per cent of operated cases. It is usually of the annular, constricting type, but may be polypoid, ulcerating, and non-constricting. Melanocarcinoma and scirrhous carcinoma, though rare, have been reported. Metastasis occurs early and, according to Mayo and Nettrour (Surg., Gynec. & Obst. **65:** 303, 1937) involves first the mesenteric lymph nodes and peritoneum, then the liver, lungs, long bones, and dura mater of the spinal cord, in the order named.

The onset of symptoms is most insidious and the duration variable, ranging from a few weeks to several years. Antedating the obstructive stage, one usually finds weakness, early fatigability, weight loss, and anemia, due in part to interference with the normal function of the small bowel, both as to motility and absorption, and in part to the occult blood loss.

As the growth increases in size and narrows the lumen of the intestine, symptoms and signs of obstruction, such as pain, abdominal distention, nausea and vomiting appear. These may be intermittent in character, usually increasing in frequency and severity as the obstruction increases. Pain may vary from a vague discomfort to severe colic, depending upon the degree of stenosis. It is usually located in the umbilical region and the lower quadrants of the abdomen. Steady pain in the epigastrium is a late symptom and probably results from metastasis to the retroperitoneal lymph nodes. Constipation is frequent, although diarrhea alternating with constipation or normal bowel movements may occur. Loss of weight is a prominent and constant finding. Visible and reverse peristalsis are occasionally seen. An abdominal mass indicates advanced disease.

A definite diagnosis can be made only roentgenologically or by exploratory operation. Until recent years, few cases were diagnosed prior to operation or autopsy. The roentgen examination is exacting and time-consuming and cannot be used routinely in many laboratories. Even in the hands of skilled roentgenologists, only about 25 per cent of these lesions can be demonstrated, but the indirect evidence may be sufficient to make a fairly accurate diagnosis in a larger percentage of cases.

The treatment of choice is radical resection, with end-to-end or lateral entero-anastomosis. If this is not practicable, a palliative entero-anastomosis around the growth is indicated. Postoperative roentgen therapy may be justified.

The prognosis, regardless of whether or not the growth is removed, is discouraging. Most of the patients now living have not had a sufficiently long follow-up to give an accurate picture of the real prognosis.

The author analyzes in detail 3 cases of adenocarcinoma of the jejunum and 4 of the ileum and includes the case histories. There were 4 males and 3 females in the series, with ages ranging from 27 to 71 years, the average age being 51 years. The duration of symptoms was from three weeks to three years or more, averaging fifteen months. The main symptoms were weight loss (varying from 10 pounds to 60 pounds and averaging 26 pounds), weakness, fatigue, abdominal pain, anorexia, vomiting, and anemia. The hemoglobin varied from 32 per cent to 89 per cent, with an average of 57 per cent; the red cell count was from 2,570,000 to 4,840,000, with an average of 3,570,000.

Resection and entero-anastomosis were done in 6 instances and palliative entero-anastomosis around the growth in a single case. Metastases to the mesenteric nodes were present in all patients, and involvement of the omentum and peritoneum was found once. There were 3 postoperative deaths. Two patients, are still living and the other 2 lived six months and two years respectively. The pathological diagnosis in each instance was adenocarcinoma.

It is important that in all patients presenting vague and indefinite gastro-intestinal symptoms and an unexplained anemia cancer of the small intestine be considered a possibility. STEPHEN N. TAGER, M.D.

Abdominal Aortic Aneurysm: Rupture Into the Jejunum Preceded by Occult Blood. Glenn I. Hiller and Richard M. Johnson. Am. J. M. Sc. **207:** 654–660, May 1944.

Rupture of an abdominal aneurysm with perforation into the gastro-intestinal tract has been reported less than 25 times. Most of the cases have involved

the duodenum. The third portion of the duodenum is relatively immobilized against the vertebral column and aorta by the pancreas, mesocolon, and ligament of Treitz. This intimate relationship probably accounts for the predilection of aneurysms in this region to rupture into this portion of the bowel. It is also probable that the pressure exerted on the relatively immobilized duodenum accounts for some of the symptoms.

In general, abdominal pain, usually epigastric, and indigestion followed by anorexia and weight loss, are the most frequent complaints. The duration of the symptoms is usually less than one year. Occult or gross blood may be found in the stools.

Roentgen evidence, when present, consists in pressure defects on adjacent structures. Fluoroscopy of the upper gastro-intestinal tract may reveal and localize an extrinsic pulsating mass. Erosion of the lumbar spine may occur, or displacement of such adjacent organs as the left side of the colon or of the left kidney. Calcification may be demonstrated in the aneurysmal sac.

A case is reported of rupture of an abdominal aneurysm in a white male aged 76, who complained of abdominal distention and pain of sudden onset five weeks before admission. Moderate tenderness was present in the epigastrium. The liver was slightly enlarged. All laboratory and roentgen studies were within normal limits, except for the persistent finding of occult blood in the stool on five occasions. Death occurred suddenly two weeks after admission. At autopsy, an arteriosclerotic abdominal aneurysm at the site of a large atheromatous ulcer was found. It had ruptured into the left retroperitoneal tissues and into the jejunum just below the duodenojejunal junction. Another small aneurysm was found involving the aortic arch.

BENJAMIN COPLEMAN, M.D.

Clinical and Radiological Observations Concerning the Large Pendulum Movement of the Colon. A. Galambos. Am. J. Digest. Dis. **11:** 151–158, May 1944.

The pendulum movement of the colon is the only one that does not move its contents. This movement is usually restricted to the transverse colon. With the hepatic and splenic flexures as fixed points, the mid transverse portion swings outward and upward. In ptotic persons this may change the position of the mid transverse colon from the region of the symphysis to the level of the xiphoid process.

In an analysis of colon movements, the patient must be in the same position and in the same phase of respiration for each film.

The author has attempted to group together under several headings the types of movements described by various writers, under different names. The small pendulum movement is one which is frequently described. It causes continuous changes in the contour of the colon and has for its purpose the mixing of the colon content. A second movement is described as "promoting peristalsis." This type of movement propels the contents along the colon by changing the form of its larger segments. The third is the *en masse* movement, which carries a large amount of fecal material along a considerable area of the colon. The fourth is the large pendulum movement first described by Rieder, which the author discusses in detail.

JOSEPH T. DANZER, M.D.

Value of the Opaque Enema and Its Modifications. Norman P. Henderson. Brit. J. Radiol. **17:** 140–149, May 1944.

On the two nights prior to an opaque enema examination, the patient should take a mild laxative. Castor oil is undesirable because of its unpleasant taste and because it frequently produces gas and spasm in the colon. Two or three hours before the examination, two plain water enemas should be given. A scout film should be made before the opaque medium is administered.

The standard procedure is still the most useful. The barium should be watched as it flows in, and the colon should be completely and evenly filled. The author discusses the application of the standard technic to the diagnosis of tumors of the large bowel and extracolonic lesions. While carcinoma of the rectum is not really within the province of the radiologist, a growth difficult to diagnose clinically may sometimes be demonstrated roentgenographically. Cases of megacolon are likely to be misleading, and an associated neoplasm may be overlooked. Early carcinomas of the bowel, occupying only a segment of the lumen, may be difficult to detect, and oblique views may be helpful. The author cites illustrative cases of these and other new growths. Examples of extracolonic conditions mentioned include ovarian tumor, bladder distention due to prostatic hypertrophy, and ruptured pelvic abscess.

Local compression combined with the standard enema may be of value. The compression should be carried out in connection with the evacuation roentgenogram, when usually only a small amount of barium is left in the bowel, and interpretation of results should be made "with the strictest reservation."

The use of air inflation following evacuation of the enema is particularly useful in the diagnosis of diverticulosis. In this connection the author describes an "anti-incontinence device" that has proved of value.

Further modifications of the standard procedure are the use of other opaque media than barium and the so-called "reduction density technic." The former seems to offer little advantage. The latter is sometimes of help in the demonstration of polyposis. The patient is first given a standard enema and allowed to evacuate it, after which a second enema, diluted 1 to 20, is administered.

In obscure cases of colitis, particularly ulcerative colitis, the inclusion of a chest film is advised to assist in the establishment or exclusion of tuberculosis as the basis of the intestinal infection.

SYDNEY J. HAWLEY, M.D.

THE SKELETAL SYSTEM

Seasonal Variations in Weight, Height, and Appearance of Ossification Centers. Earle L. Reynolds and Lester Warren Sontag. J. Pediat. **24:** 524–535, May 1944.

The authors investigated seasonal variations in weight and height and in the appearance of specific ossification centers in 133 children during the age span from twelve to sixty months. Seasonal variations, similar in the sexes, were found to exist in each of the three categories. The variation in weight was pronounced; in ossification, moderate; and in height, slight. Seasonal variations in height and ossification were parallel and opposite to the seasonal varia-

tion in weight. The period of maximum weight gain was from October to December; minimum weight gain, from April to June. The period of maximum height gain was from April to June; minimum height gain, from October to December. The period of maximum rate of appearance of ossification centers was from March to May; minimum rate of appearance, from September to November.

Fluctuations in individual growth curves, based on semiannual measurements, were shown to be sharply responsive to seasonal differences in rate of growth. Analyses of deviations in such growth curves, therefore, should take into consideration the season of the year which is covered by the interval between measurements.

Chondrodystrophia Calcificans Congenita. Maxwell P. Borovsky and Julian Arendt. J. Pediat. **24:** 558-567, May 1944.

An unusual case of congenital maldevelopment is reported in a 10-day-old infant. The knees were flexed to a 30-degree angle, and the left leg could not be extended. The findings were at first attributed to breech delivery, but re-examination in two weeks showed an aggravation of the condition and roentgenograms were made. These revealed abnormal calcification in the left knee, filling the entire upper patellar recessus and extending downward to the interarticular space. While this deposit was coherent, resembling a wax imprint of the entire capsule space, posteriorly many more round and sometimes irregular calcified bodies were seen. A few "stippled shot-like densities" were apparent in between, as well as at the foot and wrist. There was a periosteal elevation along the anterior surface of the femur. Similar changes were observed in the right knee. There were onion-peel-like periosteal elevations along both femora and a slight periosteal thickening along the tibiae. The proximal epiphyses of both humeri were well developed. Some "stippled densities" were observed beneath the epiphyseal center of the humerus. A chest film showed enlargement of the heart and thymus.

A month later, multiple stippled calcareous deposits were demonstrable in the distal row of the tarsal bones. The proximal and distal epiphyses of the tibia and femur were well developed, and the astragalus and os calcis were of normal density and showed no stippling. Changes similar to those seen in the tarsal bones were present in both wrists. The knee joints showed multiple round and partially sickle-shaped calcifications. The patellar and epiphyseal cartilage was outlined as a negative shadow by the surrounding calcium wall. The capsule appeared thickened and filled out with numerous irregular calcifications. The distal femoral epiphysis was normal but slightly smaller on the left side. The bone structure of the shafts and the epiphyseal lines appeared normal. There was a slight flaring of the metaphyseal ends of the tibia and femur.

There was no history of thyroid disturbance in the mother and no clinical or laboratory evidence of thyroid deficiency in the infant. The development of the carpal bones was normal. Kahn and Kline tests were negative. When the infant was one month old, the blood calcium was 11.9, phosphorus 4.8, and phosphatase 72 King units.

A biopsy specimen from the left knee showed large masses of calcific deposits staining a deep purplish color. They were surrounded in places by a pink, fairly homogeneous tissue which was infiltrated with large numbers of mononuclear and occasional polynuclear giant cells, engulfing the calcific deposits and having the appearance of foreign-body giant cells. The pathological diagnosis was calcification of synovia, with reactive inflammation.

Casts were applied to the legs to correct the contractures. When the patient was one year of age, x-ray films showed almost complete absorption of the calcium deposits and the appearance of normal bone formation in the metatarsal area where stippled bone was previously present.

This condition was first described by Conradi in 1914. Raap (Am. J. Roentgenol. **49:** 77, 1943) applied to it the term chondrodystrophia calcificans congenita.

Palindromic Rheumatism. A "New," Oft Recurring Disease of Joints (Arthritis, Periarthritis, Para-Arthritis) Apparently Producing No Articular Residues—Report of Thirty-Four Cases; Its Relation to "Angio-Neural Arthrosis," "Allergic Rheumatism" and Rheumatoid Arthritis. Philip S. Hench and Edward F. Rosenberg. Arch. Int. Med. **73:** 293-321, April 1944.

Palindromic rheumatism is a term applied by the authors to an unusual disease of joints and adjacent tissues, 34 cases of which have been studied in the arthritis service of the Mayo Clinic since 1928. Its outstanding features are multiple afebrile attacks of acute arthritis and periarthritis, and sometimes also of para-arthritis, with pain, swelling, redness, and disability, usually though not always confined to a single joint, in an adult of either sex. The attacks appear suddenly and develop rapidly. They generally last only a few hours or days and then disappear completely, but they recur repeatedly at short or long, irregularly spaced intervals, involving first one joint and then another. In most of the authors' cases four to six joints were affected; in others eight to eleven.

Despite the frequent recurrences and the transitory presence (in some cases at least) of an acute or subacute inflammatory polymorphonuclear exudate in the articular tissues and cavity, little or no constitutional reaction or abnormality is revealed by laboratory tests, and no significant functional, pathologic, or roentgenographic residues occur even after years of disease and scores of attacks. Of the 164 roentgenograms of various joints made in the 34 cases, 150 (91 per cent) revealed nothing significant; the remaining 14 (9 per cent) showed changes regarded as unrelated to the chief complaint.

The chief points which distinguish the cases of palindromic rheumatism from instances of rheumatoid arthritis are: (1) the totally different pattern of the arthritis (numerous short attacks and persistent functional restitution); (2) the tendency for only one or two joints to be involved in an attack; (3) the frequent isolated short attacks of para-arthritis; (4) the general absence of significant constitutional reactions; (5) the relative absence of effect of season and weather; (6) the sedimentation rate, which is relatively normal or only moderately and transiently elevated; (7) the moderate increase (rather than decrease) in blood fats; (8) the persistently negative roentgenograms, (9) the different pathologic reaction.

The absence of fever during the attacks, the short duration of the attack, the monarticular rather than polyarticular involvement, absence of hives or angio-

neurotic edema accompanying the attacks, the more advanced age of the patient, the presence of an inflammatory exudate or edema distinguish these cases from the condition described by Solis-Cohen in 1913 and termed "angio-neural arthrosis."

This condition also resembles "allergic rheumatism" described by Kahlmeter in 1939. Local redness was usually absent in Kahlmeter's cases; it was usually present in the authors' cases. Kahlmeter's patients occasionally had fever and erysipeloid rashes; none of the cases in the present series did. The frequency of the common allergic reactions was much greater in his cases than in the authors'.

The prognosis for a spontaneous cure in palindromic rheumatism is only fair. Of 27 patients whose condition is known, 15 per cent are now well, 44 per cent are improved somewhat though not notably, 26 per cent are as before, 11 per cent are somewhat worse, and 1 died of causes unrelated to the arthritis.

Osgood-Schlatter Disease. Edmond Uhry, Jr. Arch. Surg. **48:** 406–414, May 1944.

On the basis of clinical studies on 79 patients and pathologic studies of operative specimens from 20 of that number, the author concludes that Osgood-Schlatter disease develops on the basis of minor separation of the structures comprising the tibial tubercle and patellar ligament. This opinion was first advanced by Osgood and Schlatter. The characteristic pathologic changes are interpreted as being due to scar and callus formation about the fracture site. Occasionally the detached tip of the tubercle forms a pseudarthrosis. The explanation of the lack of marked separation due to quadriceps pull lies in the patellar collateral ligaments, which will preserve the function of the joint and the position of the bones even after removal of the tibial tubercle and the attachment of the patellar ligament. The age distribution of the lesion is apparently due to the weakness of the part and its susceptibility to trauma in the prepubertal period. Inflammation, osteochondritis, and endocrine disturbances seem to have no relation to this condition. Trauma is the immediate instigating factor. The most logical treatment would appear to be early immobilization, but spontaneous healing may occur.

Roentgenograms in the author's cases showed, in the first place, more or less fuzziness of the border shadow of the tibial tubercle. Sometimes it also appeared that the tongue had been pried slightly upward, its prominence being increased and the space between it and the underlying tibia being abnormally wide. Occasionally, what appeared to be a shadow of a free bony fragment could be observed lying in the ligament above and in front of the tubercle. In some instances, in which roentgenograms of serial sections were made after removal of the region *en masse*, the evidence of loss of local definition in the bone-cartilage or bone-ligament border shadows was even more apparent. In some of them the translucent or transparent shadow of a scar could be seen interposed between the bulk of the osseous apophysis and a small shadow of a flake of bone, actually avulsed forward in the process of separation. The general softness of the normal roentgen shadow of the growth zone (posterior surface of the apophyseal plate) tended to obscure the changes when they occurred in that region.

LEWIS G. JACOBS, M.D.

Eosinophilic Granuloma of Bone Presenting Neurologic Signs and Symptoms. Report of a Case. Raymond L. Osborne, Edward D. Freis, and Alfred G. Levin. Arch. Neurol. & Psychiat. **51:** 452–456, May 1944.

Following a brief review of the various features of eosinophilic granuloma and presentation of a table of differential diagnosis which includes fifteen separate osseous entities, the first reported case of eosinophilic granuloma presenting neurologic symptoms and signs is recorded.

The patient, a twenty-one-year-old soldier, complained first of facial palsy. Headache, giddiness, vomiting, deafness, tinnitus, vertigo, and deep-seated pain in the ear developed later. Abnormalities noted in the neurologic examination were confined to the cranial nerves. Roentgenograms showed solitary or confluent polycystic lesions in the left temporal bone, the mandible, the seventh cervical vertebra, the first two dorsal vertebrae, multiple ribs on both sides, the right femur, and the fifth lumbar vertebra. Histologic examination of biopsy specimens showed typical eosinophilic granuloma.

Roentgen therapy produced a favorable response.

DEPARTMENT OF ROENTGENOLOGY
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Actinomycosis of the Vertebrae. Mortimer Lubert. Am. J. Roentgenol. **51:** 669–676, June 1944.

Involvement of the vertebrae is a rather uncommon manifestation of actinomycosis. Its occurrence indicates extensive disease and the prognosis is hopeless. A review of the literature in 1935, by Meyer and Gall (J. Bone & Joint Surg. **17:** 857, 1935) resulted in a collection of 47 cases.

The roentgen findings in vertebral actinomycosis may be characteristic if not pathognomonic. Erosion of all portions of the vertebrae and adjacent ribs, including the pedicles, spine, lamina and body is a feature. The body is usually affected in its cortical portion, with periostitis as an early manifestation. The anterior surface may have a saw-tooth appearance. Reactive condensation takes place about destroyed areas and the vertebra involved may appear denser than its neighbors. The intervertebral disk is usually not affected.

In the present paper 3 cases are reported, with illustrative roentgenograms. Two of the patients showed the classical findings as described above, while one showed extensive collapse of the involved vertebral body, which is unusual. In one instance the involvement of the vertebra was apparently secondary to primary mediastinal involvement. In the second case there was an ileocecal actinomycosis with subsequent spread to the lumbar prevertebral tissues and vertebrae, and in the third case there was a primary pulmonary actinomycosis with secondary involvement of the mediastinum and vertebra. Two of the three patients gave no history of contact with grasses or cattle.

In differential diagnosis, tuberculosis and nonspecific osteomyelitis must be considered. Occasionally they may give findings similar to those seen in actinomycosis. In tuberculosis, however, involvement of the intervertebral disk with narrowing of its space and finally collapse of the vertebral bodies is the rule. In non-specific osteomyelitis, biopsy and bacteriological examination must be resorted to if the rest of the clinical picture is not conclusive. L. W. PAUL, M.D.

Madurомycosis of the Hand, With Special Reference to Heretofore Undescribed Foreign Body Granulomas Formed Around Disintegrated Chlamydospores. Douglas Symmers and Andrew Sporer. Arch. Path. **37:** 309-318, May 1944.

The case here reported is the first example of madurомycosis of the hand to be described in the United States, the second on the North American continent, and the fifth thus far recorded. It is further remarkable because of its occurrence in a man of 67 years who had never been outside the city of New York. The disease developed about three weeks after he fell on a wooden floor and sustained multiple abrasions of the palmar surface of the right hand, through which presumably the infective fungus entered.

Contrary to the opinion of Chalmers and Archibald (New Orleans M. & S. J. **70:** 455, 1917–1918), the authors believe that madurомycosis and actinomycosis are different diseases and that the histology of the former is distinctive. The granuloma of madurомycosis is formed around degenerate chlamydospores; that of actinomycosis, around ray fungi. Both are foreign body reactions but they bear only a remote resemblance to each other. The causative fungi are closely related.

The patient was admitted to the hospital in July 1937. During the preceding seven years he had suffered repeated "strokes," which left him with a weakness of the right side of the body. Two years before admission he incurred the injury to the hand described above. Two or three weeks after this the hand became swollen, and multiple pustules appeared with black dots in them. At the time of admission the hand was greatly swollen and showed many nodular formations on both the palmar and dorsal aspects. Some of these nodules contained sinuses which discharged yellowish pus and black granules. Springing from the tendon sheath of the extensor muscle of the right ring finger was a solitary cyst-like formation. Throughout the rest of the hand there were multiple subcutaneous nodules, which were moderately firm in consistency, movable, painless, and not tender. At times, during the period 1937 to 1944, acute exacerbations occurred, the nodules becoming enlarged, hot, red, and tender, and the hand as a whole increasing in size.

In 1939 roentgenograms of the hand showed areas of decalcification in the semilunar bone and os magnum and an area of ossification in the soft tissues adjacent to the metacarpophalangeal articulation of the thumb. An osteophyte was observed at the articular margin of the distal phalanx of the thumb and there were productive changes at the upper and lateral margin of the proximal phalanx of the third finger. The soft tissues of the hand and those about the proximal interphalangeal articulations of the ring and middle fingers were considerably swollen. During the next three years these changes advanced and by 1944 marked roentgen evidences of progression were present.

At the time of the report, the patient was partially paralyzed on the right side. The blood pressure varied from 220/100 to 210/150. Scattered over both surfaces of the right hand were numbers of discrete, freely movable, painless and non-tender nodules. Over many of them the skin was speckled by minute black deposits. Other nodules were surmounted by cup-like depressions from 1 to 5 mm. in diameter, encrusted by the same sort of black material. These represent the openings of fistulous tracts which formerly exuded mucopurulent material containing particles resembling grains of gunpowder. The hand was greatly enlarged, deformed, and almost useless.

The most striking histologic feature of this disease is the focal lesions which the authors call "madurомycotic granulomas" in contradistinction to the "granulomas" of actinomycosis. The granulomas of madurомycosis are of three types, of different ages, all of them built around pigmented chlamydospores, which in some places are well preserved and in other places are necrotic. One type is immature and the disintegrated chlamydospores in it are displayed against a background composed almost entirely of polymorphonuclear neutrophilic leukocytes. Encapsulation, if present, is ill defined. The second or intermediary form contains clumps of disintegrated chlamydospores and young giant cells, many of which present curious configurations and are poor in nuclear chromatin. Granulomas of this type are often encapsulated, usually by young connective tissue. The third type of granuloma is mature. The giant cells in it engage in phagocytosing waste material derived from the disintegration of chlamydospores. In some instances the mature granuloma is encapsulated by well organized connective tissue; in others, by connective tissue that is cellular and obviously young.

Boeck's Sarcoid and Systemic Sarcoidosis. (Besnier-Boeck-Schaumann Disease.) Study of 35 Cases. David Reisner. Am. Rev. Tuberc. **49:** 437–462, May 1944.

The present paper, the second in a series, deals with the clinical aspects of Boeck's sarcoid and discusses the types of lesions observed in the skin, the bones, the visceral organs, the eyes, parotid gland, and other locations. [The first paper, dealing with pulmonary lesions and involvement of the lymph nodes, was abstracted in the December 1944 issue of RADIOLOGY, page 600].

Skin lesions were present in 40 per cent of the 35 cases upon which this discussion is based, and manifest bone changes in about one-fourth. Involvement of the eye and its adnexa and of the spleen and liver was of fairly frequent occurrence. Visceral localization, especially in the lungs and lymph nodes, was far more frequent than involvement, for example, of the skin and bones, which has been considered as more characteristic. Outstanding among the general clinical characteristics of sarcoidosis are its chronic protracted course, the disproportion between the widespread anatomical involvement and the apparently good general health of the patient, as well as a pronounced tendency to spontaneous regression of the lesions in various organs.

When the bones are involved by the characteristic form of the disease, the changes are practically pathognomonic and, therefore, of great diagnostic value. The typical roentgen appearance is the osteitis tuberculosa multiplex cystoides of Jüngling. Two main types of lesions are observed: (1) the circumscribed form, consisting of sharply defined punched-out areas of rarefaction, usually situated in the medullary portion of the bone, without any accompanying reactive change; (2) the diffuse form, which produces either a lattice-like appearance of the bony structure due to multiple small, irregularly shaped areas of rarefaction, or a diffuse, finely reticulated lace-like pattern, or a combination of both. These changes are most commonly found in the bones of the hands and feet; less

often in other parts of the skeletal system. Subjective symptoms due to the osseous lesion are usually absent, although in the early stages slight change may be present. Spontaneous regression of the bone lesions may occur.

In the author's series, 40 per cent of the patients reacted positively to tuberculin tests. This appears to be considerably below the expected figure for a comparable average population, and a negative tuberculin reaction is of some value in differential diagnosis. Examinations of the sputum and gastric content for tubercle bacilli were consistently negative throughout the period of observation of these patients except those in whom manifest pulmonary tuberculosis developed during the course of observation. When the predominant location of the disease is in the visceral organs, differential diagnosis includes particularly Hodgkin's disease and disseminated hematogenous forms of tuberculosis. For a conclusive diagnosis, biopsy is often indispensable in cases of this type. Tuberculosis accounted for most of the fatal cases in the present series, 7 of the 35 patients having died. This observation, together with the occurrence of atypical cases occupying a borderline position between sarcoidosis and tuberculosis, indicates a close relationship between these two diseases. L. W. PAUL, M.D.

Traumatic Separation of the Upper Femoral Epiphysis. A Birth Injury. Putnam C. Kennedy. Am. J. Roentgenol. **51:** 707–719, June 1944.

Traumatic separation of the upper femoral epiphysis at birth is a rare lesion, probably no more than 30 cases being reported in the literature. Many of these cases are reviewed and the significant data included in the present paper. The author reports, in addition, one case of his own.

In all of the previously reported cases the separation occurred during breech presentation and extraction or version and breech extraction. In the author's case, however, there was no known difficulty in extraction of the legs, the fetus being in vertex presentation and occipito-posterior position.

Pathologically, when the upper femoral epiphysis is dislocated at birth, the cartilaginous mass as a whole is displaced medially and downwards off the curved upper surface of the shaft. The periosteum is stripped up for a variable distance along the shaft, sometimes as far as the distal end. There is hemorrhage at the site of epiphyseal separation and beneath the periosteum. The joint capsule remains intact, however, and the cartilaginous femoral head remains lodged in the acetabulum, so that no dislocation of the hip joint is present. The injury is followed by the rapid production of bony callus, which forms a large, irregular mass around the proximal end of the shaft and the displaced epiphysis. This is larger in amount, as a rule, on the upper outer aspect. Beneath the periosteum new bone formation takes place rapidly. With organization and absorption, the club-like mass gradually disappears and the femoral shaft and neck are reconstructed and remodeled.

The clinical signs of the injury consist in swelling, a slight shortening, limitation of active motion, painful passive motion, and external rotation of the thigh. There may also be discoloration, crepitus, and abduction or adduction. The roentgenographic signs consist in displacement of the proximal end of the diaphysis, upward and outward, in its relationship to the acetabulum, rapid and profuse callus formation and subperiosteal reaction around the upper end of the shaft, gradual absorption of callus and reconstruction of the femoral neck over a period of months, and premature ossification of the capital epiphysis and accelerated growth of the femoral neck on the injured side. The diagnosis is more readily made after callus becomes visible, and this usually occurs during the second week. It can be made earlier, however, if attention is paid to the relationship of the upper end of the diaphysis and the acetabular fossa. L. W. PAUL, M.D.

Lesions of the Acromioclavicular Joint Causing Pain and Disability of the Shoulder. Albert Oppenheimer. Am. J. Roentgenol. **51:** 699–706, June 1944.

The acromioclavicular joint plays an important part in determining the mobility of the shoulder girdle, and diminished mobility of this joint will interfere with most of the movements of the arm in the shoulder. For the best roentgenographic demonstration of this joint, the central ray should be perpendicular to the wing of the scapula at the level of the acromion. This may be achieved either by placing the patient supine, with the shoulder blade of the involved side flat on the table, or by having the patient stand upright with his back to the film and the shoulder drawn backwards, like a soldier standing at attention.

The normal joint space in the acromioclavicular joint varies between 2 and 5 mm. in width, as measured in roentgenograms taken at 36 in. An unusually wide joint space may indicate the presence of an articular disk, which is sometimes found as a normal variation. The articular bony surfaces are smooth and clean-cut; as seen edgewise, they may be straight, notched, concave, or convex and may differ in shape in the two joints of the same person.

In addition to fractures and dislocation, the acromioclavicular joint may be the seat of any of the various types of arthritis. Thus, tuberculous arthritis, gonorrheal arthritis, and rheumatoid and hypertrophic arthritis may be encountered, producing roentgenographic changes similar to those in other peripheral joints. Hypertrophic arthritis is the most common lesion of the acromioclavicular joint, its incidence being about twice as high as that of all other lesions combined. It produces definite disability of the shoulder. Roentgenograms show the capsule enlarged, usually with moderate widening of the joint space. In the more advanced stages, the articular surfaces are eburnated and roughened, and their margins may show bony overgrowth. The joint space may then become diminished. Irrespective of its kind and stage, arthritis of the acromioclavicular joint causes pain in the shoulder, often radiating into the arm, wrist, and fingers, with definite limitation of the movements involved in bringing the arm above shoulder level across the chest and onto the back. Pronation and supination are not limited as a rule, and this serves to distinguish involvement of this joint from that of the shoulder joint proper.

In 11 patients with chronic arthritis of this joint treated with roentgen rays, 5 became symptom-free and have remained so for over six months. Treatment consisted of doses of 50 to 70 r, with 140 kv., 0.5 mm. Cu plus 1 mm. Al filtration, 50 cm. distance, applied to fields 5 cm. square and given at intervals of four to five days. In some patients relief was noted after the second treatment, while in others six to eight treat-

ments were required to bring about complete or nearly complete relief.

It is emphasized that the clinical manifestations of the various acromioclavicular lesions may be virtually identical with those caused by bursitis, myalgia, radicular neuralgia, and traumatic injury of the shoulder girdle, and that the correct diagnosis is determined by the roentgen findings in a majority of the cases.

L. W. PAUL, M.D.

Fracture of the Carpal Scaphoid. Jeffrey M. Robertson and R. D. Wilkins. Brit. M. J. **1:** 685–687, May 20, 1944.

The authors quote Wilson [though they give no reference] as stating that 86 per cent of carpal injuries involve the scaphoid and, by contrast, Hook and Boone (U. S. Nav. M. Bull. **34:** 172, 1936), who found the incidence to be only 1 in 10. The cause is usually a fall on the outstretched hand or forced dorsiflexion of the wrist, and the symptoms are pain, swelling, and tenderness in the anatomical "snuff box." Diagnosis is made roentgenographically, four positions being recommended—anteroposterior, lateral, and two oblique. The authors' patients, 100 in number, were sailors and airmen, and the average age was 27 years.

Treatment consists in prolonged plaster-of-paris immobilization in slight dorsiflexion with the thumb in line with the long axis of the radius and slight radial deviation. For 52 of the authors' series treated within seven days of the injury, the average period of immobilization was 11.16 weeks and union was obtained in all. For 48 patients treated after greater intervals—a week to several months or even years—much longer periods of immobilization were required; the average for 13 in whom union was eventually obtained was 26 weeks. Twenty-nine of these late cases failed to show union. Operative treatment was undertaken in 12 of this number, but in only 5 was union achieved and but 3 of the 5 patients could be returned to full duty.

The importance of x-ray examination in all "sprains" of the wrist is stressed, since the weakening effect of non-union resulting from improper care may cause serious dysfunction.

Q. B. CORAY, M.D.

Unusual Pelvic Fracture. J. E. Musgrove. Canad. M. A. J. **50:** 446–447, May 1944.

A pelvic fracture is reported as unusual because of the solitary fracture line seen traversing the right inferior pubic ramus and the comparatively small degree of etiological trauma. This mishap occurred when a 40-year-old Canadian private, in good health and doing sedentary work, slipped on the ice and "did the splits." Although he fell with most of his weight on his left buttock, severe pain was experienced in the adductor region of the right thigh near the groin. A provisional diagnosis was made of strain of the right adductor longus muscle at its origin from the pubic bone. The pain persisted, however, in spite of bed rest and application of hot packs, and roentgenograms were then made. These revealed the fracture line across the pubic ramus, with two adjacent condensed lines interpreted as buckling of the cortex. Subsequent roentgen examinations showed satisfactory healing with good callus formation. The patient was discharged from the hospital after five weeks in bed and had excellent function with no pain after two more weeks.

This fracture was believed to be caused by the sudden, powerful traction of the adductor magnus. It was similar roentgenographically to the "march fractures" of the pelvis described by Nickerson (Am. J. Surg. **62:** 154, 1943. Abst. in Radiology **42:** 611, 1944).

LESTER M. J. FREEDMAN, M.D.

THE GENITO-URINARY TRACT

Bilateral Nephrolithiasis in Horseshoe Kidney. Franklin Farman. J. Urol. **51:** 447–455, May 1944.

A horseshoe kidney is more subject to complicated pathological states than is the normally formed kidney. Infection, calculosis, neoplasm, abnormal position, and aberrant blood supply are frequently associated with these malformed kidneys.

While unilateral lithiasis is apparently one of the most frequently observed concomitant lesions in the malformed kidney, the relative rarity of bilateral calculi in horseshoe kidney may be due to the fact that usually one or the other side of a fused kidney has better ureteral drainage and, consequently, less chance of urinary stasis, infection, and stone deposition.

Surgery upon the malformed kidney is dangerous, due to excessive anomalously placed blood vessels. Except for this, indications for operation are similar to those influencing decisions in the presence of a normal kidney. At times, bilateral simultaneous operation has been performed, especially through the transperitoneal approach. However, the author prefers to operate upon the "bad" kidney first to relieve acute symptoms, reserving the "good" kidney for a more selective type of operation when infection and sepsis have decreased. Conservation of renal tissue is of the utmost importance, for though the total gross volume of parenchymal tissue may equal that of two normally functioning kidneys, usually their combined function is a great deal less, due to the almost universal finding of some degree of "nephritis" within the anomalous organ.

The author reports a case of bilateral nephrolithiasis in a horseshoe kidney. Operation was performed on one side at a time, with no attempt to divide the isthmus. Bilateral nephrostomy was undertaken after the stones were removed. The clinical result was excellent.

STUART P. BARDEN, M.D.

PARASITES

Calcification in the Guinea Worm. J. S. Brocklebank. Brit. J. Radiol. **17:** 163–164, May 1944.

Infestation with the guinea worm (*Dracunculus medinensis*), common in some parts of Africa and India, occurs through drinking contaminated water. The larvae make their way from the stomach to the subcutaneous tissues usually in the feet or lower legs, where the female matures to a length of 1 to 4 feet. A small blister appears on the skin from which the larvae are discharged. The worm can usually be seen and palpated. It may be demonstrated radiographically by the injection of an opaque medium. The worm after death may become calcified. It is commonly seen as a sharply defined linear opacity, 1 to 4 mm. in width, frequently segmented. The calcification may be limited to one or more segments.

SYDNEY J. HAWLEY, M.D.

RADIOTHERAPY

NEOPLASMS

Treatment of Accessible Malignant Tumors with Short Distance Low Voltage Roentgen Rays. D. Waldron Smithers. Am. J. Roentgenol. **51:** 730–738, June 1944.

After briefly discussing the apparatus, limitations, and advantages of low-voltage short-distance roentgen therapy, the author describes the methods employed at the Royal Cancer Hospital (London). This method of treatment is limited to lesions that are directly accessible, for which it has certain advantages over radium, notably the high intensity of radiation, resulting in short treatment times, and low initial cost of the apparatus. Use is made of both the Siemens and Philips tubes. The former has a higher inherent filtration and the focal-skin distance is greater, but these factors are advantageous in some types of tumor. The author objects to the "caustic" method, whereby treatment is given at one sitting with a single massive dose. He prefers fractionation for most lesions.

For each patient a plan of treatment is outlined, with the intent to deliver an adequate tumor dose as evenly as possible to a volume that more than includes the limits of the tumor. When necessary, scale drawings are made and isodose curves applied. For the larger tumors, multiple fields are used, care being taken that there is no overlapping. When possible, two directly opposing fields are employed. This can be done in most cases of cancer of the lip, nose, ear, and anterior third of the tongue. In each case a dose is given which will result in a minimum tumor dose of 4,500–6,500 r within ten to fifteen days. The average daily dose per single field is 600 r.

The Siemens and Philips tubes have been well designed for intracavity therapy and are useful in the treatment of carcinoma of the cervix and in some intraoral tumors. The method has been used for the treatment of carcinoma of the urinary bladder after surgical exposure. Extension of this application may be expected in the future. L. W. PAUL, M.D.

Treatment of Carcinoma of the Dorsum of the Hand. P. D. Braddon. M. J. Australia **1:** 368–370, April 22, 1944.

From the surgical and radiotherapeutic point of view, carcinomas of the dorsum of the hand are classed as (1) relatively early, (2) advanced, and (3) advanced, unsuitable for irradiation.

Relatively early carcinomas are almost invariably squamous-cell; in some thousands of cases only 6 basal-cell carcinomas have been encountered. The term "early" refers not to the duration of the growth, but to the stage of advancement. Lesions in this group, measuring up to a little over 2 cm. in diameter, are best treated by surgery.

Advanced carcinomas are those measuring over 2.5 cm. in diameter. During the last eight years the author has treated 200 cases of this type. Radium or radon needles or seeds should never be implanted. All of the lesions in this group, however large, have been treated by radon molds. The total dose delivered is 6,000 gamma roentgens over a period of ten to sixteen days. Routinely 3,000 gamma roentgens are delivered over a period of seven days, at the end of which the radon is replaced by a fresh application to the mold (which is not removed) to give a further 3,000 r over the ensuing seven days. These patients are not kept in the hospital, but the hand, wrist, and forearm are splinted to ensure that the mold, often very large in area, does not move in the slightest degree. Filtration is that of radon needles, capillary, or seeds employed—namely 0.5 or 0.8 mm. of platinum equivalent. Excellent results have been obtained in all cases, with good function, regardless of the extent of the lesion, with not a single case of radionecrosis, recurrence, or metastasis.

The author treated with surgery three cases too extensive for treatment with the radon mold. One patient had axillary metastases and died, in spite of amputation of the hand and excision of the axillary nodes. Partial amputation was performed in the second case, and axillary nodes were excised but histologically these showed no malignant growth. The third patient had radionecrosis and recurrence following x-ray treatment elsewhere. The result of partial amputation in this case was disappointing, because of sloughing of the tissues and poor healing.

Concentration Method of Radiotherapy for Cancer of the Mouth, Pharynx and Larynx: Report of Progress. Max Cutler. Am. J. Roentgenol. **51:**739–746, June 1944.

Further experiences with the so-called "concentration method" of radiotherapy for cancers of the mouth, pharynx and larynx (J. A. M. A. **117:** 1607, 1941. Abst. in Radiology **38:** 635, 1942) are reported. Five technics have been employed since 1938 in an effort to determine the comparative value of roentgen rays and radium, the optimum voltage, optimum roentgen intensity, optimum daily and total doses, optimum treatment time, and the optimum number and size of fields. These are as follows.

(1) Telecurietherapy, with twelve treatment days, a single constant portal, and a total dose of 120,000 mg.-hr. This is used for lesions of the alveolar ridge and floor of the mouth in which the disease is entirely or mainly unilateral.

(2) Roentgen therapy, with twelve treatment days, two constant portals, and doses of 7,600 to 8,400 r. This is being used for lesions of the soft and hard palates.

(3) Roentgen therapy, with eleven treatment days, single diminishing portal, dose of 5,400 r. This is used in intrinsic carcinoma of the larynx when radiotherapy has been decided upon as the method of treatment.

(4) Roentgen therapy, interrupted method, with ten treatment days, two fields, diminishing portals, dose of 7,700 r. This technic is used in the more advanced cases of intrinsic carcinoma of the larynx, in which it is desired to know the radiosensitivity of the lesion. (See Cutler: Arch. Otolaryng. **39:** 53, 1944. Abst. in Radiology **43:** 315, 1944).

(5) Roentgen therapy, with eighteen treatment days, single diminishing portal, dose of 6,500 r. This is used in extrinsic carcinomas of the larynx and has been the most effective method so far observed for this type of lesion.

The basis of the method of concentration is the use of large daily doses over a comparatively short treatment period (ten to eighteen days). The total dose is

sufficient to produce an "epithelitis" and occasionally an epidermitis. The method has resulted in regression, disappearance, and apparent cures of lesions that had failed to respond to the divided dose technic. There is some evidence that gradually increasing the daily dose and decreasing the size of the field is of advantage.

The results in 290 cases treated between April 1938 and April 1943 are recorded in tabular form. Illustrative cases are included for each of the treatment technics described. L. W. PAUL, M.D.

Indications for and Effects of Irradiation of the Pituitary Gland: Symposium. Edgar A. Kahn, A. C. Crooke, and J. F. Bromley. Brit. J. Radiol. **17:** 133–139, May 1944.

This Symposium opens with a paper by Major Kahn of the U. S. Army Medical Corps. He presents the views of various authorities as to the irradiation of chromophobe adenomas of the pituitary. Of Cushing's large series (as reported by Henderson: Brit. J. Surg. **26:** 811, 1939), only 10 patients received preoperative roentgen therapy, and in none of these was operation delayed more than a month. In only one was significant improvement observed following irradiation. Postoperative irradiation, however, was found to have a very favorable effect in decreasing the rapidity and percentage of recurrences. Sosman (personal communication to the writer) allows a six-month period to determine the effectiveness of the roentgen rays if the patient is not growing worse. He believes that satisfactory remissions will follow irradiation in about 50 per cent of cases. Dyke and Davidoff also recommended a trial of irradiation for chromophobe adenomas, to be followed by operation if necessary. Davidoff believes that 40 to 60 per cent of these tumors will respond favorably to roentgen therapy. Dott and Peet, on the other hand, regard the chromophobe adenomas as insensitive to radiation. Kahn's own opinion is that in comparatively early cases a fair trial should be given x-ray therapy. If vision is borderline or deteriorating when the patient is first seen, operation should not be delayed. Irradiation should always be done postoperatively.

Crooke opened his contribution to the Symposium with the statement that, while the effect of deep x-ray therapy upon the size of pituitary tumors is established, the effect on the output of pituitary hormones is questionable. Pituitary glands examined after tumor doses of 1,600 r have shown no cytological changes, though functional change may, of course, occur in the absence of cytological alterations. It is difficult to evaluate changes in secretory activity due to irradiation, since normally the pituitary varies in its output and there are no accurate methods of assay. A possible method is a study of carbohydrate metabolism. Since patients with acromegaly and basophilism commonly have an associated diabetes mellitus, they are particularly suitable for such a study, the alteration of insulin requirements after irradiation functioning as an index of its effectiveness. In a case of acromegaly reported here, however, the diabetic condition became steadily worse, in spite of a total tumor dose of 2,540 r, which would thus appear to be inadequate.

The fundamental pathology in basophilism is different. Here there is a hyaline change in the basophile cells of the anterior lobe. The disease is one of hyperfunction, and irradiation would thus be expected to relieve the symptoms. Reports in the literature, however, have not shown satisfactory results. In 2 recorded cases improvement was obtained by radon implantation, and Crooke presents an additional case which, though refractory to x-ray therapy, responded promptly to the insertion of radon seeds. In view of these results, he believes that x-rays could accomplish good results if sufficiently large doses could be administered without damage to the surrounding structures.

Bromley, whose paper concludes the Symposium, feels that the radiation therapist is often asked to do too much and often too little in the treatment of pituitary tumors: too much in the sense that to obtain cure requires very large doses, which are difficult and dangerous to apply; too little in the sense that he is not often enough called upon to relieve symptoms, which can be accomplished with smaller doses. The best results are obtained in eosinophile adenomas, but even in chromophobe tumors, if they are diagnosed early, a trial of irradiation is justified.

There is a field of treatment of pituitary conditions apart from true tumors that merits further attention. There is, for example, a mild form of Cushing's syndrome —amenorrhea or dysmenorrhea, mental stolidity, a tendency to virilism, and a coarse dry skin—that responds promptly to x-ray therapy. The headaches associated with hypertrophy of the pituitary at the menopause can also be relieved by small doses of x-ray to the gland. SYDNEY J. HAWLEY, M.D.

Discussion on the Treatment of Carcinoma of the Oesophagus. Hermon Taylor, W. M. Levitt, M. Lederman, *et al.* Proc. Roy. Soc. Med. **37:** 331–340, May 1944.

In this discussion on carcinoma of the esophagus, radiotherapy received due consideration.

Levitt referred to a series of 7 cases previously recorded (Proc. Soc. Roy. Med. **27:** 368, 1934) in which a strip-field method of deep x-ray therapy had been followed by disappearance of the growth. A subsequent study of this group, however, showed 5 deaths as a result of pulmonary lesions attributable to the irradiation and 1 from recurrent carcinoma. The remaining patient died of cardiac failure, and autopsy showed a brown atrophy of the heart muscle which was believed to be a radiation effect.

In spite of improvements in technic, Levitt still finds it impossible to reproduce his earlier results without injury to the lungs. He has been most successful with growths of the upper third of the esophagus showing large fleshy fungations into the lumen, and he believes that "with suitable dosage and distribution of radiations to the esophagus, and disregarding the lung, a very remarkable percentage of primary regressions can be obtained." Irradiation is contraindicated in the presence of mediastinitis, pulmonary extension and secondary deposits, as well as in all cases involving the lower third of the esophagus.

Lederman discussed radium therapy. Tumors of the cervical esophagus, with or without pharyngeal involvement he considers suitable for teleradium therapy, provided they do not extend below the first thoracic vertebra. Mid-esophageal growths may be treated by radium bougie or radon implantation. Lederman regards the former method as preferable and outlines the technic. Guisez is said to have had excellent results with this procedure. Lederman, however, can report only one survival for as long as two and a half years in a series of 33 cases, but he regards

the palliative effects as of "incalculable value." He mentions a case treated by Mr. Lawrence Abel with a survival period of ten years and death at the end of that time from intercurrent disease. Cardio-esophageal tumors are unsuitable for treatment either by teleradium or radium bougie, which cannot deliver an adequate dose to the gastric part of the neoplasm. Implantation of radium seeds has been attempted, but accurate distribution of the dose is difficult, and the method is recommended only as a last resort.

D. W. Smithers favored roentgen therapy over surgery and presented his own results. He had treated over 100 cases with x-rays, 80 of them more than two years earlier, and had seen no instance of fibrosis of the lung in spite of the fact that 20 of these patients had lived one year or longer. Three patients, in two of whom microscopic proof of carcinoma was obtained, were symptom-free more than five years after treatment. Of 32 patients who completed treatment prior to the war, 30 experienced marked relief of symptoms, and 11 had remained symptom-free for varying periods.

Various aspects of the subject were taken up by other participants in the discussion.

Value of Surgery and X-Ray Treatments in Carcinoma of the Breast. Roswell T. Pettit. Illinois M. J. **85:** 244–247, May 1944.

Statistical reports on carcinoma of the breast show a conflict of opinion, often confusing, in the evaluation of the results of treatment. This is due in part to the wide variation in the course of the disease and in classification of operable and inoperable cases.

The author quotes the statistics of Lazarus-Barlow, showing a 12 per cent five-year survival rate in 651 untreated cases of carcinoma of the breast, for use as a base line in evaluating results of treatment. In 10,000 cases treated surgically in 23 widely distributed clinics, the five-year survival reported varies from 16 to 52 per cent with an average of about 29 per cent. This is definite evidence of the value of surgical treatment. The wide variation in the percentages of survival may be due largely to differences in selection of cases for operation.

Operability depends upon the stage of the disease, especially the presence or absence of axillary involvement. The five-year survival reported in cases without involvement of axillary nodes varies from 61 to 74.2 per cent.

Irradiation followed by radical amputation has been preferred by many. Statistical reports on preoperative irradiation, however, have been somewhat disappointing, and it has the disadvantage of delaying surgery several weeks. The results reported are slightly better than by surgery alone. Irradiation following radical mastectomy has shown better results. Adair reports 76.8 per cent five-year survivals in 95 cases without axillary involvement, and 41.8 per cent in 177 cases with extension to the axilla (J. A. M. A. **121:** 553, 1943. Abst. in Radiology **41:** 311, 1943). Since it has been shown by serial sections that most cases of carcinoma of the breast have axillary metastases, even if not palpable, postoperative irradiation is advocated for all cases. It is often overlooked that technic, skill, diligence, and good equipment are as important in the application of x-ray therapy as in the surgical treatment.

The author reports 149 cases of carcinoma of the breast treated postoperatively by irradiation with a five-year survival of 58.3 per cent. The presence or absence of axillary metastases was not determined in all cases, but the majority of patients had axillary involvement.

X-ray therapy properly administered in sufficient dosage is an extremely valuable adjunct to surgery. The x-ray procedure is not well standardized, but with improvements that have been made and are being made it is reasonable to believe that five-year results in patients now being treated will be better than those previously obtained. H. H. WRIGHT, M.D.

Medical Progress. Gynecology: Carcinoma of the Cervix. Joe V. Meigs. New England J. Med. **230:** 577–582, 607–613, May 11 and May 18, 1944.

This is a rather long but excellent discussion of carcinoma of the cervix. Irradiation has been of great help in treating cervical cancer, the percentage of cure being about the same in all the large collections of statistics. Since there seems to be a limit to the cure and salvage by irradiation, the author advocates radical operative procedures with removal of cervix, uterus, tubes and ovaries, and the iliac lymph nodes. With experience, the operative mortality has decreased.

Many good points are made. It is suggested that the radiologist be given a freer hand in determining the method and amount of treatment. Many cancers of the cervix could be prevented by total hysterectomy. The Schiller test, colposcopy, and the newly advocated stained vaginal smear are all good procedures and should be used. Biopsy is still the best means of diagnosis and should be employed oftener and earlier. It is possible to take a specimen from a carcinoma of the cervix and not obtain malignant tissue. With the Schiller stain, the area for biopsy is well defined.

Classification according to the League of Nations formula is being more widely accepted and practised, although that of Schmitz or the American College of Surgeons is probably more convenient. The microscopic grading of tumors is not of great advantage either in treatment or prognosis.

Cancer of the cervical stump would not occur if every hysterectomy were a total hysterectomy.

A good discussion of cervical cancer in pregnancy is included. JOHN B. MCANENY, M.D.

Carcinoma of the Bladder: An Improved Technique for the Cystoscopic Implantation of Radium Element. Thomas D. Moore. J. Urol. **51:** 496–504, May 1944.

In the past, treatment of infiltrating carcinoma of the bladder has been unsatisfactory, except for those series in which radium or radon therapy was included in the management.

The author, in 1938, first advocated a method of cystoscopic introduction of radium needles, which were left in place for twenty-four to seventy-two hours and then removed cystoscopically. This procedure is best suited for lesions of low-grade malignancy and occasional early cases of grade III and IV tumors. It is especially well adapted to aged patients because of the relatively low morbidity. The method is restricted to lesions accessible to direct cystoscopic view, namely, the trigone, lateral base, posterior wall, and posterior part of the lateral walls. It cannot be used for growths involving the dome, anterior wall, and anterior part of the lateral walls.

The advantages of radium needles over radon seeds are twofold. First, there is no foreign body left in a region which is subject to infection. In the second place, it is cheaper to use radium needles. The author's method is no more difficult than the implantation of radon seeds.

A cystogram is first made in order to determine the extent of infiltration. Then, under low spinal or pentothal sodium anesthesia, the Braasch direct-vision cystoscope is introduced and the lesion is electrocoagulated if sessile in type. Radium needles containing 1, 3, or 5 mg. and measuring 10 to 17 mm. in length are inserted into the lesion 1.5 cm. apart. This is accomplished by means of the author's special radium needle introducer. In men, the needles are identified by lead shot, but in women the silk threads are brought out through the urethra. The cystoscope is removed and a 75 c.c. Foley catheter is inserted. This is distended with 120 c.c. of sterile water to protect the opposing wall of the bladder and prevent accidental loss of the radium. Bladder irrigations are carried out through the catheter.

After forty-eight to seventy-two hours the cystoscope is reintroduced in male patients and the needles are removed by picking up the lead shot with a Braasch specimen forceps. In women, the catheter is removed and the needles are withdrawn by traction on the silk threads.

The author discusses the question of biopsy. He is convinced that this should be done routinely at the first cystoscopy.

In 11 of 96 cases in the author's files, this method was used (in 7 women and 4 men). All the lesions were grade II or III. Six patients are alive from one month to four and a half years. Five are dead after living six months to six years. JOSEPH SELMAN, M.D.

Cancer of the Female Urethra. W. G. Cuscaden. M. J. Australia **1:** 487–489, May 27, 1944.

Fourteen cases of urethral cancer in women are presented. The average age of the patients was fifty-two years. Of the 14 patients, 6 are well at present, and one, after living twelve years, cannot be traced. Hemorrhage was the most consistent and in many cases the only symptom. Difficulty in micturition occurred only in advanced cases. Pain was a late symptom. Thirteen of the lesions were epitheliomata; one was an adenocarcinoma.

With slight variation, the same dosage and technic were used in all cases. Gold needles 2.5 cm. in length, containing 5 mc. of radon, screened by 0.8 mm. platinum, were inserted so that the treated tissue extended between concentric cylinders 7.5 and 17.5 mm. in diameter and 2.5 cm. in length. The needles were left in place for eight days. The average minimum dose around the outside of the treated tissue was 19,000 r, while the maximum dose was approximately 40,000 r 1.0 mm. away from the surface of the needle.

Some pain and frequency of micturition followed treatment, but usually subsided in six to eight weeks. Abundant fluids and citrate of potash were given during this period. Sloughing was not serious except in one case, in which two lots of irradiation were given. Radon in vaseline was used once a week in this case (eight hours) and was thought to have helped in healing the condition. With this single exception, stricture was not a serious complication.

Osteogenic Osteolytic Sarcoma of the Os Pubis. Sidney T. Friedman. Am. J. Surg. **64:** 248–253, May 1944.

A case of osteogenic osteolytic sarcoma of the os pubis is reported, in which the only treatment possible was biopsy followed by roentgen irradiation. The patient lived approximately three and a half years after the institution of treatment.

Hemangioblastoma of the Medulla—Lindau's Disease: Response to Radiation Therapy. Mervyn H. Hirschfeld. J. Nerv. & Ment. Dis. **99:** 656–659, May 1944.

No record of any attempted treatment for hemangioblastoma of the medulla or spinal cord could be found in the literature by the author. In the case described radiation therapy was attended by surprisingly good results.

This patient was a 21-year-old male whose chief complaint on admission was dysphagia. In the previous three years, he had gradually lost the sight of his left eye due to hemangioblastoma of the retina (von Hippel's disease) and glaucoma. The right eye was normal except for slight nystagmus on upward and lateral gaze. The left facial muscles contracted and relaxed more slowly than the right, but no definite paralysis was noted. Speech was somewhat labored due to accumulation of saliva in the throat. Numbness and tingling were present in the left upper and lower extremities but the patient could identify objects through tactile sensation and there was no alteration of temperature sense. Electroencephalography showed changes indicating a lesion in the right parietal and posterior temporal region. A pneumoencephalogram was normal but was followed by a severe reaction and complete inability to swallow, which lasted for forty-eight hours. The absence of definite cerebellar signs and the prominence of hiccups and dysphagia indicated that the major lesion was in the medulla.

Since operation was inadvisable, radiation therapy was administered over the occiput and upper cervical spine through right and left lateral portals. A total of 1,475 r, measured in air, was delivered in 22 sessions in 26 days (200 kv. constant potential, total filtration of 0.75 mm. Cu plus 2.0 mm. Al, 50 cm. target-skin distance, with an output of 53 r per minute). The calculated mid-line tumor dose was 2,160 r. The patient became worse during treatment, being confined to bed because of instability of his legs. Immobility of the pharynx and upper esophagus developed, being demonstrable by fluoroscopy. One week after the termination of treatment, there was marked decrease of salivation with rapid progressive improvement of symptoms. Four months after treatment, tingling in the ulnar three fingers of the left hand was the sole symptom and slow reaction of the left facial musculature was the only abnormal neurologic finding. Enucleation of the left eye was advised but was refused. Because of the usual multiplicity of lesions in this condition and their variable rate of development the author does not regard this case as closed.

LESTER M. J. FREEDMAN, M.D.

Hemangioma of the Testis. A. H. Kleiman. J. Urol. **51:** 548–549, May 1944.

The author reports a case of testicular tumor in a 51-year-old white carpenter, preoperatively diagnosed

as malignant but found histologically to be benign. The chief complaint was slow enlargement of the left scrotal contents, without tenderness but producing a dragging sensation of the scrotum. The mass was first noticed a year before admission.

The left testis was three times its normal size and only slightly sensitive to pressure. The vas deferens and epididymis were normal, as were results of all laboratory studies. The patient received a total of 5,300 r to the mass between Aug. 27 and Sept. 28, 1940, which was well tolerated and caused the mass to shrink to less than one-half its former size. Orchiectomy was performed three weeks later.

On gross examination, the split left testis was found to contain in its center a dark red nodule 2 cm. in diameter. Microscopically, it was seen to be surrounded by a thick wall of fibrous tissue, while its substance was composed of anastomosing capillaries, venules, and small arteries distended with erythrocytes. There was a delicate fibrous tissue stroma between the blood spaces, and the surrounding seminiferous tubules were atrophic. The pathologic diagnosis was hemangioma cavernosum. The postoperative course was uneventful.

Hemangioma of the testis is a rare condition. Study of several sections of the tumor has failed to reveal any malignant process. N. P. SALNER, M.D.

EXPERIMENTAL STUDIES

Experimental Hypoproteinemia and Edema. Studies of Intestinal Absorption and Intestinal Roentgenologic Characteristics. Argyl J. Beams, Alfred H. Free, and Jack R. Leonards. Arch. Int. Med. **73:** 397–402, May 1944.

Hypoproteinemia with edema was produced in 5 dogs by means of plasmapheresis. The intestinal absorption of galactose and aminoacetic acid was studied by improved tolerance tests in these animals and was found to be unaffected to any significant degree.

Roentgen studies of the gastro-intestinal tract following the administration of barium showed no alteration in gastric emptying and intestinal motility as a result of the hypoproteinemia and edema. In some of the films of the small intestine during edema there were moderate clumping of the barium and segmentation. These phenomena were also noted in the studies on normal animals, although they occurred less frequently.

Studies of plasma volume and available (thiocyanate) fluid volume indicated that during edema the plasma volume is not significantly altered but that the available (thiocyanate) fluid volume is noticeably increased.

The rate of metabolism of galactose and aminoacetic acid was not altered by hypoproteinemia and edema.

Area Factor in Roentgen Irradiation. H. C. Goldberg. Arch. Dermat. & Syph. **49:** 346–347, May 1944.

In a series of experiments the author has measured the amount of irradiation necessary to cause an erythema in areas having diameters from 1 to 10 cm. Using 120 kv., 6 ma., 10 cm. target-skin distance, and no filter, which gives a half-value layer of 1.9 mm. Al, he has in chart form given the number of units necessary for an erythema dose.

It was found that 3,060 r were needed in treating an area 1 mm. in diameter in order to get an erythema effect on the skin, whereas 510 r were sufficient to get the same effect on an area 10 mm. in diameter. A series of tests was made to determine the area factor in relation to dosage, the number of skin units necessary to cause an erythema. JOSEPH T. DANZER, M.D.

Effect of Iodized Poppyseed Oil and Iodine-Chlorine in Peanut Oil in the Subarachnoid Space of Animals. Edwin Boldrey and Robert B. Aird. J. Nerv. & Ment. Dis. **99:** 521–533, May 1944.

Search for a substitute radiopaque oil was prompted by the disappearance from the market of 40 per cent iodized poppyseed oil (lipiodol) following the fall of France. Lipoiodine (60 per cent solution of diiodobrassidic acid in sesame oil) and iodochlorol (27 per cent iodine, 7.5 per cent chlorine, in peanut oil) were considered for study, but since the former proved the more irritating in preliminary studies, it was discarded.

Six parallel experiments were attempted on large dogs, averaging over 18 kg. in weight. Cisternal fluid was removed from the animals under local anesthesia and 2 c.c. of lipiodol or of iodochlorol were injected into the subarachnoid space. Spinal fluid was removed at intervals for cell counts and for Pandy reactions. Some animals were autopsied within a week and others within three months following one injection. Four dogs had a repeat injection one week following the first, 2 of these being autopsied 4 days later and the remaining 2 three months later. A third group was similarly studied after single injections of the oils combined with 2 c.c. of blood.

The reaction of the animals to iodochlorol was comparable to and generally slightly less in degree than the reaction to lipiodol. The irritative phenomena were found to be definitely increased in the animals that received the blood injection. The total cell counts of the spinal fluid were elevated, reaching a peak in twenty-four to forty-eight hours following the oil injection and gradually decreasing over a four-week period. The repeat injection prompted a secondary rise in the count. The differential count showed a predominance of polymorphonuclears with a shift to a lymphocytic reaction during the first week after injection of iodochlorol. Pandy responses were all positive.

Microscopic studies showed early changes in the meninges to be minimal in degree and extent. These were somewhat more marked after a repeated dose of oil. The addition of blood to the opaque media increased the irritating effect from the very beginning. Adjacent ganglion cells showed changes in their nuclei and tigroid substances in many instances. Advanced proliferative and fibrotic changes in the meninges were noted in the animals sacrificed late. The oils were walled-off in a mesh-work of cysts and fibers in the subarachnoid space, extending even to the caudal sac in some of the dogs. Less fibroblastic and collagenous response was evoked by iodochlorol than by lipiodol. This was also true of the chronic inflammatory cell reaction. No abnormalities were noted in the ganglion cells in this "late" group, indicating that the changes noted in the "early" groups were reversible.

The authors believe that early removal of these oils from the subarachnoid space is highly desirable.

LESTER M. J. FREEDMAN, M.D.